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<b>(54) Title:</b> NOVEL MOLECULES OF THE TANGO-77 RELATED PROTEIN FAMILY AND USES THEREOF  <b>(57) Abstract</b>  Novel Tango-77 polypeptides, proteins, and nucleic acid molecules are disclosed. In addition to isolated, full-length Tango-77 proteins, the invention further provides isolated Tango-77 fusion proteins, antigenic peptides and anti-Tango-77 antibodies. The invention also provides Tango-77 nucleic acid molecules, recombinant expression vectors containing a nucleic acid molecule of the invention, host cells into which the expression vectors have been introduced and non-human transgenic animals in which a Tango-77 gene has been introduced or disrupted. Diagnostic, screening and therapeutic methods utilizing compositions of the invention are also provided.		

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NOVEL MOLECULES OF THE TANGO-77 RELATED PROTEIN  
FAMILY AND USES THEREOF

Background of the Invention

The polypeptide cytokine interleukin-1 (IL-1) is a critical mediator of inflammatory and overall immune response. To date, three members of the IL-1 family, IL-1 $\alpha$ , IL-1 $\beta$  and IL-1ra (Interleukin-1 receptor antagonist) have been isolated and cloned. IL-1 $\alpha$  and IL-1 $\beta$  are proinflammatory cytokines which elicit biological responses, whereas IL-1ra is an antagonist of IL-1 $\alpha$  and IL-1 $\beta$  activity. Two distinct cell-surface receptors have been identified for these ligands, the type I IL-1 receptor (IL-1RtI) and type II IL-1 receptor (IL-1RtII). Recent results suggest that the IL-1RtI is the receptor responsible for transducing a signal and producing biological effects.

As mentioned above, IL-1 is a key mediator of the host inflammatory response. While inflammation is an important homeostatic mechanism, aberrant inflammation has the potential for inducing damage to the host. Elevated IL-1 levels are known to be associated with a number of diseases particularly autoimmune diseases and inflammatory disorders.

Since IL-1ra is a naturally occurring inhibitor of IL-1, IL-1ra can be used to limit the aberrant and potentially deleterious effects of IL-1. In experimental animals, pretreatment with IL-1ra has been shown to prevent death resulting from lipopolysaccharide-induced sepsis. The relative absence of IL-1ra has also been suggested to play a role in human inflammatory bowel disease.

Summary of the Invention

The present invention is based, at least in part, on the discovery of a gene encoding Tango-77, a secreted

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protein that is predicted to be a member of the cytokine superfamily. The Tango-77 cDNA described below (SEQ ID NO:1) has three possible open reading frames. The first potential open reading frame encompasses 534 nucleotides  
5 extending from nucleotide 356 to nucleotide 889 of SEQ ID NO:1 (SEQ ID NO:3) and encodes a 178 amino acid protein (SEQ ID NO:2). This protein may include a predicted signal sequence of about 63 amino acids (from about amino acid 1 to about amino acid 63 of SEQ ID NO:2 (SEQ ID  
10 NO:4) and a predicted mature protein of about 115 amino acids (from about amino acid 64 to amino acid 178 of SEQ ID NO:2 (SEQ ID NO:5)).

The second potential open reading frame encompasses 498 nucleotides extending from nucleotide 389  
15 to nucleotide 889 of SEQ ID NO:1 (SEQ ID NO:6) and encodes a 167 amino acid protein (SEQ ID NO:7). This protein may include a predicted signal sequence of about 52 amino acids (from about amino acid 1 to about amino acid 52 of SEQ ID NO:7 (SEQ ID NO:8)) and a predicted  
20 mature protein of about 115 amino acids (from about amino acid 52 to amino acid 167 of SEQ ID NO:7 (SEQ ID NO:9)).

The third potential open reading frame encompasses 408 nucleotides extending from nucleotide 481 to nucleotide 889 of SEQ ID NO:1 (SEQ ID NO:10) and encodes  
25 a 136 amino acid protein (SEQ ID NO:11). This protein includes a predicted signal sequence of about 21 amino acids (from about amino acid 1 to about amino acid 21 of SEQ ID NO:11 (SEQ ID NO:12)) and a predicted mature protein of about 115 amino acids (from about amino acid  
30 22 to amino acid 136 of SEQ ID NO:11 (SEQ ID NO:13)).

As used herein, the terms "Tango-77", "Tango-77 protein", "Tango-77 polypeptide" and the like, can refer and polypeptide produced by the cDNA of SEQ ID NO:1 including any and all of the Tango-77 gene products  
35 described above.



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Tango-77 is expected to inhibit inflammation and play a functional role similar to that of secreted IL-1ra. For example, it is expected that Tango-77 may bind to the IL-1 receptor, thus blocking receptor  
5 activation by inhibiting the binding of IL-1 $\alpha$  and IL-1 $\beta$  to the receptor. Alternatively, Tango-77 may inhibit inflammation through another pathway, for example, by binding to a novel receptor. Accordingly, Tango-77 may be useful as a modulating agent in regulating a variety  
10 of cellular processes including acute and chronic inflammation, e.g., asthma, chronic myelogenous leukemia, rheumatoid arthritis, psoriasis and inflammatory bowel disease.

In one aspect, the invention provides isolated  
15 nucleic acid molecules encoding Tango-77 or biologically active portions thereof, as well as nucleic acid fragments suitable as primers or hybridization probes for the detection of Tango-77.

The invention encompasses methods of diagnosing  
20 and treating patients who are suffering from a disorder associated with an abnormal level (undesirably high or undesirably low) of inflammation, abnormal activity of the IL-1 receptor complex, or abnormal activity of IL-1, by administering a compound that modulates the expression  
25 of Tango-77 (at the DNA, mRNA or protein level, e.g., by altering mRNA splicing) or by altering the activity of Tango-77. Examples of such compounds include small molecules, antisense nucleic acid molecules, ribozymes, and polypeptides.

30 The invention features a nucleic acid molecule which is at least 45% (e.g., 55%, 65%, 75%, 85%, 95%, or 98%) identical to the nucleotide sequence shown in SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, the nucleotide sequence of the cDNA insert of the plasmid

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deposited with ATCC as Accession Number (the "cDNA of ATCC 98807"), or a complement thereof.

The invention features a nucleic acid molecule which includes a fragment of at least 100 (e.g., 250,  
5 325, 350, 375, 400, 425, 450, 500, 550, 600, 650, 700, 800, 900, or 989) nucleotides of the nucleotide sequence shown in SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, the nucleotide sequence of the cDNA ATCC 98807, or a complement thereof.

10 The invention also features a nucleic acid molecule which includes a nucleotide sequence encoding a protein having an amino acid sequence that is at least 45% (55%, 65%, 75%, 85%, 95%, or 98%) identical to the amino acid sequence of SEQ ID NO:2, SEQ ID NO:5, SEQ ID  
15 NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, or the amino acid sequence encoded by the cDNA of ATCC 98807.

In a preferred embodiment, a Tango-77 nucleic acid molecule has the nucleotide sequence shown in SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10 or the  
20 nucleotide sequence of the cDNA of ATCC 98807.

Also within the invention is a nucleic acid molecule which encodes a fragment of a polypeptide having the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID  
25 NO:11, SEQ ID NO:12, SEQ ID NO:13, wherein the fragment includes at least 15 (e.g., 25, 30, 50, 100, 150, or 178) contiguous amino acids of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or the polypeptide  
30 encoded by the cDNA of ATCC Accession Number 98807.

The invention includes a nucleic acid molecule which encodes a naturally occurring allelic variant of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8,  
35 SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or

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an amino acid sequence encoded by the cDNA of ATCC  
Accession Number 98807, wherein the nucleic acid molecule  
hybridizes to a nucleic acid molecule comprising SEQ ID  
NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, or a  
5 complement thereof under stringent conditions.

Also within the invention are: an isolated  
Tango-77 protein having an amino acid sequence that is at  
least about 45%, preferably 65%, 75%, 85%, 95%, or 98%  
identical to the amino acid sequence of SEQ ID NO:5, SEQ  
10 ID NO:9 or SEQ ID NO:13 (mature human Tango-77), or the  
amino acid sequence of SEQ ID NO:2, SEQ ID NO:7 or SEQ ID  
NO:11 (immature human Tango-77).

Also within the invention are: an isolated  
Tango-77 protein which is encoded by a nucleic acid  
15 molecule having a nucleotide sequence that is at least  
about 65%, preferably 75%, 85%, or 95% identical to SEQ  
ID NO:3, SEQ ID NO:6, SEQ ID NO:10 or the cDNA of ATCC  
98807; and an isolated Tango-77 protein which is encoded  
by a nucleic acid molecule having a nucleotide sequence  
20 which hybridizes under stringent hybridization conditions  
to a nucleic acid molecule having the nucleotide sequence  
of SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, the non-coding  
strand of the cDNA of ATCC 98807, or the complement  
thereof.

25 Also within the invention is a polypeptide which  
is a naturally occurring allelic variant of a polypeptide  
that includes the amino acid sequence of SEQ ID NO:2, SEQ  
ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID  
NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or an  
30 amino acid sequence encoded by the cDNA insert of the  
plasmid deposited with ATCC as Accession Number 98807,  
wherein the polypeptide is encoded by a nucleic acid  
molecule which hybridizes to a nucleic acid molecule  
comprising SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID

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NO:10 or the complement thereof under stringent conditions.

Another embodiment of the invention features Tango-77 nucleic acid molecules which specifically detect  
5 Tango-77 nucleic acid molecules relative to nucleic acid molecules encoding other members of the cytokine superfamily. For example, in one embodiment, a Tango-77 nucleic acid molecule hybridizes under stringent conditions to a nucleic acid molecule comprising the  
10 nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, the cDNA of ATCC 98807, or a complement thereof. In another embodiment, the Tango-77 nucleic acid molecule is at least 300 (325, 350, 375, 400, 425, 450, 500, 550, 600, 650, 700, 800, 900, or 989)  
15 nucleotides in length and hybridizes under stringent conditions to a nucleic acid molecule comprising the nucleotide sequence shown in SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, the cDNA of ATCC 98807, or a complement thereof. In yet another embodiment, the  
20 invention provides an isolated nucleic acid molecule which is antisense to the coding strand of a Tango-77 nucleic acid.

Another aspect of the invention provides a vector, e.g., a recombinant expression vector, comprising a  
25 Tango-77 nucleic acid molecule of the invention. In another embodiment, the invention provides a host cell containing such a vector. The invention also provides a method for producing Tango-77 protein by culturing, in a suitable medium, a host cell of the invention containing  
30 a recombinant expression vector such that a Tango-77 protein is produced.

Another aspect of this invention features isolated or recombinant Tango-77 proteins and polypeptides. Preferred Tango-77 proteins and polypeptides possess at  
35 least one biological activity possessed by naturally

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occurring human Tango-77, e.g., (i) the ability to interact with proteins in the Tango-77 signalling pathway (ii) the ability to interact with a Tango-77 ligand or receptor; or (iii) the ability to interact with an  
5 intracellular target protein, (iv) the ability to interact with a protein involved in inflammation and (v) the ability to bind the IL-1 receptor. Other activities include the induction and suppression of polypeptide interleukins, cytokines and growth factors.

10 The Tango-77 proteins of the present invention, or biologically active portions thereof, can be operably linked to a non-Tango-77 polypeptide (e.g., heterologous amino acid sequences) to form Tango-77 fusion proteins. The invention further features antibodies that  
15 specifically bind Tango-77 proteins, such as monoclonal or polyclonal antibodies. In addition, the Tango-77 proteins or biologically active portions thereof can be incorporated into pharmaceutical compositions, which optionally include pharmaceutically acceptable carriers.

20 In another aspect, the present invention provides a method for detecting the presence of Tango-77 activity or expression in a biological sample by contacting the biological sample with an agent capable of detecting an indicator of Tango-77 activity or expression such that  
25 the presence of Tango-77 activity or expression is detected in the biological sample.

In another aspect, the invention provides a method for modulating Tango-77 activity comprising contacting a cell with an agent that modulates (inhibits or  
30 stimulates)

Tango-77 activity or expression such that Tango-77 activity or expression in the cell is modulated. In one embodiment, the agent is an antibody that specifically binds to Tango-77 protein. In another embodiment, the

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agent modulates expression of Tango-77 by modulating transcription of a Tango-77 gene, splicing of a Tango-77 mRNA, or translation of a Tango-77 mRNA. In yet another embodiment, the agent is a nucleic acid molecule having a nucleotide sequence that is antisense to the coding strand of the Tango-77 mRNA or the Tango-77 gene.

In one embodiment, the methods of the present invention are used to treat a subject having a disorder characterized by aberrant Tango-77 protein activity or nucleic acid expression by administering an agent which is a Tango-77 modulator to the subject. In one embodiment, the Tango-77 modulator is a Tango-77 protein. In another embodiment, the Tango-77 modulator is a Tango-77 nucleic acid molecule. In other embodiments, the Tango-77 modulator is a peptide, peptidomimetic, or other small molecule. In a preferred embodiment, the disorder characterized by aberrant Tango-77 protein or nucleic acid expression can include chronic and acute inflammation.

The present invention also provides a diagnostic assay for identifying the presence or absence of a genetic lesion or mutation characterized by at least one of: (i) aberrant modification or mutation of a gene encoding a Tango-77 protein; (ii) mis-regulation of a gene encoding a Tango-77 protein; and (iii) aberrant post-translational modification of a Tango-77 protein, wherein a wild-type form of the gene encodes a protein with a Tango-77 activity.

In another aspect, the invention provides a method for identifying a compound that binds to or modulates the activity of a Tango-77 protein. In general, such methods entail measuring a biological activity of a Tango-77 protein in the presence and absence of a test compound and identifying those

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compounds which alter the activity of the Tango-77 protein.

The invention also features methods for identifying a compound which modulates the expression of Tango-77 by measuring the expression of Tango-77 in the presence and absence of a compound.

Other features and advantages of the invention will be apparent from the following detailed description and claims.

10                   Brief Description of the Drawings

Figure 1 depicts the cDNA sequence (SEQ ID NO:1) of Tango-77. The Tango-77 cDNA has three possible open reading frames which encode the amino acid sequence (SEQ ID NO:2, SEQ ID NO:7 and SEQ ID NO:11) of human Tango-77. 15 The three potential open reading frames of SEQ ID NO:1 extend from: (1) nucleotide 356 to nucleotide 889 (SEQ ID NO:3); (2) nucleotide 389 to nucleotide 889 (SEQ ID NO:6); and (3) nucleotide 481 to nucleotide 889 (SEQ ID NO:10).

20                   Figure 2 depicts an alignment of an amino acid sequence of Tango-77 (T77; SEQ ID NO:2) with IL-1RA (SEQ ID NO:14), and IL-1 $\beta$  (SEQ ID NO:15).

Figure 3 depicts the genomic sequence of BAC1 (SEQ ID NO:16).

25                   Figure 4 depicts the genomic sequence of BAC2 (SEQ ID NO:17).

Figure 5 depicts an amino acid sequence of an alternatively spliced form of Tango-77 (SEQ ID NO:2) as predicted by Procrustes (T77-procrustes; SEQ ID NO:18).

30                   Figure 6 depicts an alignment of an amino acid sequence of an alternatively spliced form of Tango-77 (T77-procrustes; SEQ ID NO:18) with Tango-77 (SEQ ID NO:2).

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Figure 7 depicts an alignment of an amino acid sequence of an alternatively spliced form of Tango-77 (T77-procrustes; SEQ ID NO:18) with IL-1ra (SEQ ID NO:14), and IL-1 $\beta$  (SEQ ID NO:15).

5                   Detailed Description of the Invention

The present invention is based on the discovery of a cDNA molecule encoding human Tango-77, a member of the cytokine superfamily. The cDNA molecule encoding human Tango-77 has three possible open reading frames. The  
10 three possible nucleotide open reading frames for human Tango-77 protein are shown in Figure 1 (SEQ ID NO:3, SEQ ID NO:6 and SEQ ID NO:10). The predicted amino acid sequence for the three possible Tango-77 immature proteins are also shown in  
15 Figure 1 (SEQ ID NO:2, SEQ ID NO:7 or SEQ ID NO:11) and three possible mature proteins are also shown in Figure 1 (SEQ ID NO:5, SEQ ID NO:9 and SEQ ID NO:13).

The Tango-77 cDNA of Figure 1 (SEQ ID NO:1), which is approximately 989 nucleotides long including  
20 untranslated regions, encodes a protein amino acid having a molecular weight of approximately 19 kDa, 18 kDa, or 14.9 kDa (excluding post-translational modifications) and the possible mature form of the protein has a molecular weight of 13 kDa. A plasmid containing a cDNA encoding  
25 human Tango-77 (with the cDNA insert name of Of fthx077) was deposited with American Type Culture Collection (ATCC), 10801 University Boulevard, Manassas, Virginia 20110-2209 on July 2, 1998 and assigned Accession Number 98807. This deposit will be maintained under the terms  
30 of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure. This deposit was made merely as a convenience for those of skill in the art and is not an



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admission that a deposit is required under 35 U.S.C. §112.

Human Tango-77 is one member of a family of molecules (the "Tango-77 family") having certain conserved structural and functional features. The term "family," when referring to the protein and nucleic acid molecules of the invention, is intended to mean two or more proteins or nucleic acid molecules having a common structural domain and having sufficient amino acid or nucleotide sequence identity as defined herein. Such family members can be naturally occurring and can be from either the same or different species. For example, a family can contain a first protein of human origin and a homologue of that protein of murine origin, as well as a second, distinct protein of human origin and a murine homologue of that protein. Members of a family may also have common functional characteristics.

As used interchangeably herein a "Tango-77 activity", "biological activity of Tango-77" or "functional activity of Tango-77", refers to an activity exerted by a Tango-77 protein, polypeptide or nucleic acid molecule on a Tango-77 responsive cell as determined *in vivo*, or *in vitro*, according to standard techniques. A Tango-77 activity can be a direct activity, such as an association with a second protein, or an indirect activity, such as a cellular signaling activity mediated by interaction of the Tango-77 protein with a second protein. In a preferred embodiment, a Tango-77 activity includes at least one or more of the following activities: (i) the ability to interact with proteins in the Tango-77 signalling pathway (ii) the ability to interact with a Tango-77 ligand or receptor; or (iii) the ability to interact with an intracellular target protein, (iv) the ability to interact with a protein involved in

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inflammation, and (v) the ability to bind the IL-1 receptor.

Accordingly, another embodiment of the invention features isolated Tango-77 proteins and polypeptides  
5 having a Tango-77 activity.

Yet another embodiment of the invention features Tango-77 molecules which contain a signal sequence. Generally, a signal sequence (or signal peptide) is a peptide containing about 21 to 63 amino acids which  
10 occurs at the extreme N-terminal end of a secretory protein. The native Tango-77 signal sequence (SEQ ID NO:4, SEQ ID NO:8, or SEQ ID NO:12) can be removed and replaced with a signal sequence from another protein. In certain host cells (e.g., mammalian host cells),  
15 expression and/or secretion of Tango-77 can be increased through use of a heterologous signal sequence. For example, the gp67 secretory sequence of the baculovirus envelope protein can be used as a heterologous signal sequence. Alternatively, the native Tango-77 signal  
20 sequence can itself be used as a heterologous signal sequence in expression systems, e.g., to facilitate the secretion of a protein of interest.

Various aspects of the invention are described in further detail in the following subsections.

#### 25 I. Isolated Nucleic Acid Molecules

One aspect of the invention pertains to isolated nucleic acid molecules that encode Tango-77 proteins or biologically active portions thereof, as well as nucleic acid molecules sufficient for use as hybridization probes  
30 to identify Tango-77-encoding nucleic acids (e.g., Tango-77 mRNA) and fragments for use as PCR primers for the amplification or mutation of Tango-77 nucleic acid molecules. As used herein, the term "nucleic acid molecule" is intended to include DNA molecules (e.g.,

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cDNA or genomic DNA) and RNA molecules (e.g., mRNA) and analogs of the DNA or RNA generated using nucleotide analogs. The nucleic acid molecule can be single-stranded or double-stranded, but preferably is double-stranded DNA.

An "isolated" nucleic acid molecule is one which is separated from other nucleic acid molecules which are present in the natural source of the nucleic acid. Preferably, an "isolated" nucleic acid is free of sequences (preferably protein encoding sequences) which naturally flank the nucleic acid (i.e., sequences located at the 5' and 3' ends of the nucleic acid) in the genomic DNA of the organism from which the nucleic acid is derived. For example, in various embodiments, the isolated Tango-77 nucleic acid molecule can contain less than about 5 kb, 4 kb, 3 kb, 2 kb, 1 kb, 0.5 kb or 0.1 kb of nucleotide sequences which naturally flank the nucleic acid molecule in genomic DNA of the cell from which the nucleic acid is derived. Moreover, an "isolated" nucleic acid molecule, such as a cDNA molecule, can be substantially free of other cellular material, or culture medium when produced by recombinant techniques, or substantially free of chemical precursors or other chemicals when chemically synthesized.

A nucleic acid molecule of the present invention, e.g., a nucleic acid molecule having the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, the cDNA of ATCC 98807, or a complement of any of these nucleotide sequences, can be isolated using standard molecular biology techniques and the sequence information provided herein. Using all or a portion of the nucleic acid sequences of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, the cDNA of ATCC 98807, or the complement thereof as a hybridization probe, Tango-77 nucleic acid molecules can be isolated using standard

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hybridization and cloning techniques (e.g., as described in Sambrook et al., eds., *Molecular Cloning: A Laboratory Manual*, 2nd ed., Cold Spring Harbor Laboratory, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 1989).

A nucleic acid of the invention can be amplified using cDNA, mRNA or genomic DNA as a template and appropriate oligonucleotide primers according to standard PCR amplification techniques. The nucleic acid so amplified can be cloned into an appropriate vector and characterized by DNA sequence analysis. Furthermore, oligonucleotides corresponding to Tango-77 nucleotide sequences can be prepared by standard synthetic techniques, e.g., using an automated DNA synthesizer.

In another preferred embodiment, an isolated nucleic acid molecule of the invention comprises a nucleic acid molecule which is a complement of the nucleotide sequence shown in SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10 the cDNA of ATCC 98807, or a portion thereof. A nucleic acid molecule which is complementary to a given nucleotide sequence is one which is sufficiently complementary to the given nucleotide sequence that it can hybridize to the given nucleotide sequence thereby forming a stable duplex.

Moreover, the nucleic acid molecule of the invention can comprise only a portion of a nucleic acid sequence encoding Tango-77, for example, a fragment which can be used as a probe or primer or a fragment encoding a biologically active portion of Tango-77. The nucleotide sequence determined from the cloning of the human Tango-77 gene allows for the generation of probes and primers designed for use in identifying and/or cloning Tango-77 homologues in other cell types, e.g., from other tissues, as well as Tango-77 homologues from other mammals. The probe/primer typically comprises

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substantially purified oligonucleotide. The oligonucleotide typically comprises a region of nucleotide sequence that hybridizes under stringent conditions to at least about 12, preferably about 25,  
5 more preferably about 50, 75, 100, 125, 150, 175, 200, 250, 300, 350 or 400 consecutive nucleotides of the sense or anti-sense sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, or the cDNA of ATCC 98807. Alternatively, the oligonucleotide can typically comprise  
10 a region of nucleotide sequence that hybridizes under stringent conditions to at least about 12, preferably about 25, more preferably about 50, 75, 100, 125, 150, 175, 200, 250, 300, 350 or 400 consecutive nucleotides of the sense or anti-sense sequence of a naturally occurring  
15 mutant of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, or the cDNA of ATCC 98807.

Probes based on the human Tango-77 nucleotide sequence can be used to detect transcripts or genomic sequences encoding the same or identical proteins. The  
20 probe comprises a label group attached thereto, e.g., a radioisotope, a fluorescent compound, an enzyme, or an enzyme co-factor. Such probes can be used as a part of a diagnostic test kit for identifying cells or tissues which mis-express a Tango-77 protein, such as by  
25 measuring a level of a Tango-77-encoding nucleic acid in a sample of cells from a subject, e.g., detecting Tango-77 mRNA levels or determining whether a genomic Tango-77 gene has been mutated or deleted.

A nucleic acid fragment encoding a "biologically  
30 active portion of Tango-77" can be prepared by isolating a portion of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10 or the nucleotide sequence of the cDNA of ATCC 98807 which encodes a polypeptide having a Tango-77 biological activity, expressing the encoded portion of  
35 Tango-77 protein (e.g., by recombinant expression in

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vitro) and assessing the activity of the encoded portion of Tango-77.

The invention further encompasses nucleic acid molecules that differ from the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, or the cDNA of ATCC 98807 due to degeneracy of the genetic code and thus encode the same Tango-77 protein as that encoded by the nucleotide sequence shown in SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, or the cDNA of ATCC 98807.

In addition to the human Tango-77 nucleotide sequence shown in SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, or the cDNA of ATCC 98807, it will be appreciated by those skilled in the art that DNA sequence polymorphisms that lead to changes in the amino acid sequences of Tango-77 may exist within a population (e.g., the human population). Such genetic polymorphism in the Tango-77 gene may exist among individuals within a population due to natural allelic variation. An allele is one of a group of genes which occur alternatively at a given genetic locus. As used herein, the term "allelic variant" refers to a nucleotide sequence which occurs at a Tango-77 locus or to a polypeptide encoded by the nucleotide sequence. As used herein, the terms "gene" and "recombinant gene" refer to nucleic acid molecules comprising an open reading frame encoding a Tango-77 protein, preferably a mammalian Tango-77 protein. Such natural allelic variations can typically result in 1-5% variance in the nucleotide sequence of the Tango-77 gene. Alternative alleles can be identified by sequencing the gene of interest in a number of different individuals. This can be readily carried out by using hybridization probes to identify the same genetic locus in a variety of individuals. Any and all such nucleotide variations and resulting amino acid polymorphisms or variations in

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Tango-77 that are the result of natural allelic variation and that do not alter the functional activity of Tango-77 are intended to be within the scope of the invention.

Moreover, nucleic acid molecules encoding Tango-77  
5 proteins from other species (Tango-77 homologues), which have a nucleotide sequence which differs from that of a human Tango-77, are intended to be within the scope of the invention. Nucleic acid molecules corresponding to natural allelic variants and homologues of the Tango-77  
10 cDNA of the invention can be isolated based on their identity to the human Tango-77 nucleic acids disclosed herein using the human cDNAs, or a portion thereof, as a hybridization probe according to standard hybridization techniques under stringent hybridization conditions.

15 Accordingly, in another embodiment, an isolated nucleic acid molecule of the invention is at least 300 (325, 350, 375, 400, 425, 450, 500, 550, 600, 650, 700, 800, or 989) nucleotides in length and hybridizes under stringent conditions to the nucleic acid molecule  
20 comprising the nucleotide sequence, preferably the coding sequence, of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, or the cDNA of ATCC 98807.

As used herein, the term "hybridizes under stringent conditions" is intended to describe conditions  
25 for hybridization and washing under which nucleotide sequences at least 60% (65%, 70%, preferably 75%) identical to each other typically remain hybridized to each other. Such stringent conditions are known to those skilled in the art and can be found in *Current Protocols*  
30 *in Molecular Biology*, John Wiley & Sons, N.Y. (1989), 6.3.1-6.3.6. A preferred, non-limiting example of stringent hybridization conditions are hybridization in 6X sodium chloride/sodium citrate (SSC) at about 45°C, followed by one or more washes in 0.2X SSC, 0.1% SDS at  
35 50-65°C. Preferably, an isolated nucleic acid molecule

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of the invention that hybridizes under stringent conditions to the sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, the cDNA of ATCC 98807, or the complement thereof, corresponds to a naturally-occurring  
5 nucleic acid molecule. As used herein, a "naturally-occurring" nucleic acid molecule refers to an RNA or DNA molecule having a nucleotide sequence that occurs in nature (e.g., encodes a natural protein).

In addition to naturally-occurring allelic  
10 variants of the Tango-77 sequence that may exist in the population, the skilled artisan will further appreciate that changes can be introduced by mutation into the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10 or the cDNA of ATCC 98807, thereby  
15 leading to changes in the amino acid sequence of the encoded Tango-77 protein, without altering the biological activity of the Tango-77 protein. Amino acid residues that are not conserved or only semiconserved among Tango-77 of various species may be non-essential for activity  
20 and thus would likely be targets for alteration. Alternatively, one can make nucleotide substitutions leading to amino acid substitutions at "non-essential" amino acid residues. A "non-essential" amino acid residue is a residue that can be altered from the wild-  
25 type sequence of Tango-77 (e.g., the sequence of SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11 or SEQ ID NO:13) without altering the biological activity, whereas an "essential" amino acid residue is required for biological activity. For example, amino  
30 acid residues that are conserved among the Tango-77 proteins of various species may be essential for activity and thus would not likely be targets for alteration, unless one wishes to reduce or alter Tango-77 activity.

Accordingly, another aspect of the invention  
35 pertains to nucleic acid molecules encoding Tango-77



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proteins that contain changes in amino acid residues that are not essential for activity. Such Tango-77 proteins differ in amino acid sequence from SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13 yet retain biological activity. In one embodiment, the isolated nucleic acid molecule includes a nucleotide sequence encoding a protein that includes an amino acid sequence that is at least about 45% identical, 65%, 75%, 85%, 95%, or 98% identical to the amino acid sequence of SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13.

An isolated nucleic acid molecule encoding a Tango-77 protein having a sequence which differs from that of SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13 can be created by introducing one or more nucleotide substitutions, additions or deletions into the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, or the cDNA of ATCC 98807 such that one or more amino acid substitutions, additions or deletions are introduced into the encoded protein. Mutations can be introduced by standard techniques, such as site-directed mutagenesis and PCR-mediated mutagenesis. Preferably, conservative amino acid substitutions are made at one or more predicted non-essential amino acid residues. A "conservative amino acid substitution" is one in which the amino acid residue is replaced with an amino acid residue having a similar side chain. Families of amino acid residues having similar side chains have been defined in the art. These families include amino acids with basic side chains (e.g., lysine, arginine, histidine), acidic side chains (e.g., aspartic acid, glutamic acid), uncharged polar side chains (e.g., glycine, asparagine, glutamine, serine, threonine, tyrosine, cysteine), nonpolar side chains (e.g., alanine,

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valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan), beta-branched side chains (e.g., threonine, valine, isoleucine) and aromatic side chains (e.g., tyrosine, phenylalanine, tryptophan, histidine).

5 Thus, a predicted nonessential amino acid residue in Tango-77 is preferably replaced with another amino acid residue from the same side chain family. Alternatively, mutations can be introduced randomly along all or part of a Tango-77 coding sequence, such as by saturation  
10 mutagenesis, and the resultant mutants can be screened for Tango-77 biological activity to identify mutants that retain activity. Following mutagenesis, the encoded protein can be expressed recombinantly and the activity of the protein can be determined.

15 In a preferred embodiment, a mutant Tango-77 protein can be assayed for: (1) the ability to form protein:protein interactions with proteins in the Tango-77 signalling pathway; (2) the ability to bind a Tango-77 ligand or receptor; or (3) the ability to bind  
20 to an intracellular target protein or (4) the ability to interact with a protein involved in inflammation or (5) the ability to bind the IL-1 receptor. In yet another preferred embodiment, a mutant Tango-77 can be assayed for the ability to modulate inflammation, asthma,  
25 autoimmune diseases, and sepsis.

The present invention encompasses antisense nucleic acid molecules, i.e., molecules which are complementary to a sense nucleic acid encoding a protein, e.g., complementary to the coding strand of a double-  
30 stranded cDNA molecule or complementary to an mRNA sequence. Accordingly, an antisense nucleic acid can hydrogen bond to a sense nucleic acid. The antisense nucleic acid can be complementary to an entire Tango-77 coding strand, or to only a portion thereof, e.g., all or  
35 part of the protein coding region (or open reading

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frame). An antisense nucleic acid molecule can be antisense to a noncoding region of the coding strand of a nucleotide sequence encoding Tango-77. The noncoding regions ("5' and 3' untranslated regions") are the 5' and 5 3' sequences which flank the coding region and are not translated into amino acids.

Given the coding strand sequences encoding Tango-77 disclosed herein (e.g., SEQ ID NO:3, SEQ ID NO:5, or SEQ ID NO:8), antisense nucleic acids of the invention 10 can be designed according to the rules of Watson and Crick base pairing. The antisense nucleic acid molecule can be complementary to the entire coding region of Tango-77 mRNA, but more preferably is an oligonucleotide which is antisense to only a portion of the coding or 15 noncoding region of Tango-77 mRNA. For example, the antisense oligonucleotide can be complementary to the region surrounding the translation start site of Tango-77 mRNA, e.g., an oligonucleotide having the sequence 5'-TGCAACTTTTACAGGAAACAC-3' (SEQ ID NO:19) or 20 5'-CCTCACTTTTACCCGAGACTC-3' (SEQ ID NO:20) or 5'-GACGGGTGGTACTTAAACAA-3' (SEQ ID NO:21). An antisense oligonucleotide can be, for example, about 5, 10, 15, 20, 25, 30, 35, 40, 45 or 50 nucleotides in length. An antisense nucleic acid of the invention can be 25 constructed using chemical synthesis and enzymatic ligation reactions using procedures known in the art. For example, an antisense nucleic acid (e.g., an antisense oligonucleotide) can be chemically synthesized using naturally occurring nucleotides or variously 30 modified nucleotides designed to increase the biological stability of the molecules or to increase the physical stability of the duplex formed between the antisense and sense nucleic acids, e.g., phosphorothioate derivatives and acridine substituted nucleotides can be used. 35 Examples of modified nucleotides which can be used to

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generate the antisense nucleic acid include 5-fluorouracil, 5-bromouracil, 5-chlorouracil, 5-iodouracil, hypoxanthine, xanthine, 4-acetylcytosine, 5-(carboxyhydroxymethyl) uracil, 5-carboxymethylaminomethyl-2-thiouridine, 5-carboxymethylaminomethyluracil, dihydrouracil, beta-D-galactosylqueosine, inosine, N6-isopentenyladenine, 1-methylguanine, 1-methylinosine, 2,2-dimethylguanine, 2-methyladenine, 2-methylguanine, 3-methylcytosine, 5-methylcytosine, N6-adenine, 7-methylguanine, 5-methylaminomethyluracil, 5-methoxyaminomethyl-2-thiouracil, beta-D-mannosylqueosine, 5'-methoxycarboxymethyluracil, 5-methoxyuracil, 2-methylthio-N6-isopentenyladenine, uracil-5-oxyacetic acid (v), wybutoxosine, pseudouracil, queosine, 2-thiocytosine, 5-methyl-2-thiouracil, 2-thiouracil, 4-thiouracil, 5-methyluracil, uracil-5-oxyacetic acid methylester, uracil-5-oxyacetic acid (v), 5-methyl-2-thiouracil, 3-(3-amino-3-N-2-carboxypropyl) uracil (acp3)w, and 2,6-diaminopurine. Alternatively, the antisense nucleic acid can be produced biologically using an expression vector into which a nucleic acid has been subcloned in an antisense orientation (i.e., RNA transcribed from the inserted nucleic acid will be of an antisense orientation to a target nucleic acid of interest, described further in the following subsection).

The antisense nucleic acid molecules of the invention are typically administered to a subject or generated *in situ* such that they hybridize with or bind to cellular mRNA and/or genomic DNA encoding a Tango-77 protein to thereby inhibit expression of the protein, e.g., by inhibiting transcription and/or translation. The hybridization can be by conventional nucleotide complementarity to form a stable duplex, or, for example, in the case of an antisense nucleic acid molecule which

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binds to DNA duplexes, through specific interactions in the major groove of the double helix. An example of a route of administration of antisense nucleic acid molecules of the invention includes direct injection at a tissue site. Alternatively, antisense nucleic acid molecules can be modified to target selected cells and then administered systemically. For example, for systemic administration, antisense molecules can be modified such that they specifically bind to receptors or antigens expressed on a selected cell surface, e.g., by linking the antisense nucleic acid molecules to peptides or antibodies which bind to cell surface receptors or antigens. The antisense nucleic acid molecules can also be delivered to cells using the vectors described herein. To achieve sufficient intracellular concentrations of the antisense molecules, vector constructs in which the antisense nucleic acid molecule is placed under the control of a strong pol II or pol III promoter are preferred.

20 An antisense nucleic acid molecule of the invention can be an  $\alpha$ -anomeric nucleic acid molecule. An  $\alpha$ -anomeric nucleic acid molecule forms specific double-stranded hybrids with complementary RNA in which, contrary to the usual  $\beta$ -units, the strands run parallel to each other (Gaultier et al. (1987) *Nucleic Acids Res.* 15:6625-6641). The antisense nucleic acid molecule can also comprise a 2'-o-methylribonucleotide (Inoue et al. (1987) *Nucleic Acids Res.* 15:6131-6148) or a chimeric RNA-DNA analogue (Inoue et al. (1987) *FEBS Lett.* 215:327-330).

The invention also encompasses ribozymes. Ribozymes are catalytic RNA molecules with ribonuclease activity which are capable of cleaving a single-stranded nucleic acid, such as an mRNA, to which they have a complementary region. Thus, ribozymes (e.g., hammerhead

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ribozymes (described in Haselhoff and Gerlach (1988) *Nature* 334:585-591)) can be used to catalytically cleave Tango-77 mRNA transcripts to thereby inhibit translation of Tango-77 mRNA. A ribozyme having specificity for a  
5 Tango-77-encoding nucleic acid can be designed based upon the nucleotide sequence of a Tango-77 cDNA disclosed herein (e.g., SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10). For example, a derivative of a *Tetrahymena* L-19 IVS RNA can be constructed in which the nucleotide  
10 sequence of the active site is complementary to the nucleotide sequence to be cleaved in a Tango-77-encoding mRNA. See, e.g., Cech et al. U.S. Patent No. 4,987,071; and Cech et al. U.S. Patent No. 5,116,742. Alternatively, Tango-77 mRNA can be used to select a  
15 catalytic RNA having a specific ribonuclease activity from a pool of RNA molecules. See, e.g., Bartel and Szostak (1993) *Science* 261:1411-1418.

The invention also encompasses nucleic acid molecules which form triple helical structures. For  
20 example, Tango-77 gene expression can be inhibited by targeting nucleotide sequences complementary to the regulatory region of the Tango-77 (e.g., the Tango-77 promoter and/or enhancers) to form triple helical structures that prevent transcription of the Tango-77  
25 gene in target cells. See generally, Helene (1991) *Anticancer Drug Des.* 6(6):569-84; Helene (1992) *Ann. N.Y. Acad. Sci.* 660:27-36; and Maher (1992) *Bioassays* 14(12):807-15.

In preferred embodiments, the nucleic acid  
30 molecules of the invention can be modified at the base moiety, sugar moiety or phosphate backbone to improve, e.g., the stability, hybridization, or solubility of the molecule. For example, the deoxyribose phosphate backbone of the nucleic acids can be modified to generate  
35 peptide nucleic acids (see Hyrup et al. (1996) *Bioorganic*

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& *Medicinal Chemistry* 4(1): 5-23). As used herein, the terms "peptide nucleic acids" or "PNAs" refer to nucleic acid mimics, e.g., DNA mimics, in which the deoxyribose phosphate backbone is replaced by a pseudopeptide backbone and only the four natural nucleobases are retained. The neutral backbone of PNAs has been shown to allow for specific hybridization to DNA and RNA under conditions of low ionic strength. The synthesis of PNA oligomers can be performed using standard solid phase peptide synthesis protocols as described in Hyrup et al. (1996) *supra*; Perry-O'Keefe et al. (1996) *Proc. Natl. Acad. Sci. USA* 93: 14670-675.

PNAs of Tango-77 can be used in therapeutic and diagnostic applications. For example, PNAs can be used as antisense or antigene agents for sequence-specific modulation of gene expression by, e.g., inducing transcription or translation arrest or inhibiting replication. PNAs of Tango-77 can also be used, e.g., in the analysis of single base pair mutations in a gene by, e.g., PNA directed PCR clamping; as artificial restriction enzymes when used in combination with other enzymes, e.g., S1 nucleases (Hyrup (1996) *supra*; or as probes or primers for DNA sequence and hybridization (Hyrup (1996) *supra*; Perry-O'Keefe et al. (1996) *Proc. Natl. Acad. Sci. USA* 93: 14670-675).

In another embodiment, PNAs of Tango-77 can be modified, e.g., to enhance their stability or cellular uptake, by attaching lipophilic or other helper groups to PNA, by the formation of PNA-DNA chimeras, or by the use of liposomes or other techniques of drug delivery known in the art. For example, PNA-DNA chimeras of Tango-77 can be generated which may combine the advantageous properties of PNA and DNA. Such chimeras allow DNA recognition enzymes, e.g., RNase H and DNA polymerases, to interact with the DNA portion while the PNA portion

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would provide high binding affinity and specificity. PNA-DNA chimeras can be linked using linkers of appropriate lengths selected in terms of base stacking, number of bonds between the nucleobases, and orientation  
5 (Hyrup (1996) *supra*). The synthesis of PNA-DNA chimeras can be performed as described in Hyrup (1996) *supra* and Finn et al. (1996) *Nucleic Acids Res.* 24(17):3357-63. For example, a DNA chain can be synthesized on a solid support using standard phosphoramidite coupling chemistry  
10 and modified nucleoside analogs. Compounds such as 5'-(4-methoxytrityl)amino-5'-deoxy-thymidine phosphoramidite can be used as a link between the PNA and the 5' end of DNA (Mag et al. (1989) *Nucleic Acid Res.* 17:5973-88). PNA monomers are then coupled in a stepwise manner to  
15 produce a chimeric molecule with a 5' PNA segment and a 3' DNA segment (Finn et al. (1996) *Nucleic Acids Res.* 24(17):3357-63). Alternatively, chimeric molecules can be synthesized with a 5' DNA segment and a 3' PNA segment (Peterser et al. (1975) *Bioorganic Med. Chem. Lett.*  
20 5:1119-11124).

In other embodiments, the oligonucleotide may include other appended groups such as peptides (e.g., for targeting host cell receptors *in vivo*), or agents facilitating transport across the cell membrane (see,  
25 e.g., Letsinger et al. (1989) *Proc. Natl. Acad. Sci. USA* 86:6553-6556; Lemaitre et al. (1987) *Proc. Natl. Acad. Sci. USA* 84:648-652; PCT Publication No. WO 88/09810) or the blood-brain barrier (see, e.g., PCT Publication No. WO 89/10134). In addition, oligonucleotides can be  
30 modified with hybridization-triggered cleavage agents (see, e.g., Krol et al. (1988) *Bio/Techniques* 6:958-976) or intercalating agents (see, e.g., Zon (1988) *Pharm. Res.* 5:539-549). To this end, the oligonucleotide may be conjugated to another molecule, e.g., a peptide,



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hybridization triggered cross-linking agent, transport agent, hybridization-triggered cleavage agent, etc.

## II. Isolated Tango-77 Proteins and Anti-Tango-77 Antibodies

5           One aspect of the invention pertains to isolated Tango-77 proteins, and biologically active portions thereof, as well as polypeptide fragments suitable for use as immunogens to raise anti-Tango-77 antibodies. In one embodiment, native Tango-77 proteins can be isolated  
10 from cells or tissue sources by an appropriate purification scheme using standard protein purification techniques. In another embodiment, Tango-77 proteins are produced by recombinant DNA techniques. Alternative to recombinant expression, a Tango-77 protein or polypeptide  
15 can be synthesized chemically using standard peptide synthesis techniques.

          An "isolated" or "purified" protein or biologically active portion thereof is substantially free of cellular material or other contaminating proteins from  
20 the cell or tissue source from which the Tango-77 protein is derived, or substantially free of chemical precursors or other chemicals when chemically synthesized. The language "substantially free of cellular material" includes preparations of Tango-77 protein in which the  
25 protein is separated from cellular components of the cells from which it is isolated or recombinantly produced. Thus, Tango-77 protein that is substantially free of cellular material includes preparations of Tango-77 protein having less than about 30%, 20%, 10%, or  
30 5% (by dry weight) of non-Tango-77 protein (also referred to herein as a "contaminating protein"). When the Tango-77 protein or biologically active portion thereof is recombinantly produced, it is also preferably substantially free of culture medium, i.e., culture

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medium represents less than about 20%, 10%, or 5% of the volume of the protein preparation. When Tango-77 protein is produced by chemical synthesis, it is preferably substantially free of chemical precursors or other chemicals, i.e., it is separated from chemical precursors or other chemicals which are involved in the synthesis of the protein. Accordingly such preparations of Tango-77 protein have less than about 30%, 20%, 10%, 5% (by dry weight) of chemical precursors or non-Tango-77 chemicals.

Biologically active portions of a Tango-77 protein include peptides comprising amino acid sequences sufficiently identical to or derived from the amino acid sequence of the Tango-77 protein (e.g., the amino acid sequence shown in SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13), which include fewer amino acids than the full length Tango-77 proteins, and exhibit at least one activity of a Tango-77 protein. Typically, biologically active portions comprise a domain or motif with at least one activity of the Tango-77 protein. A biologically active portion of a Tango-77 protein can be a polypeptide which is, for example, 10, 25, 50, 100 or more amino acids in length.

Moreover, other biologically active portions, in which other regions of the protein are deleted, can be prepared by recombinant techniques and evaluated for one or more of the functional activities of a native Tango-77 protein.

Preferred Tango-77 protein has the amino acid sequence shown of SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13. Other useful Tango-77 proteins are substantially identical to SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13 and retain the functional activity of the protein of SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13 yet differ in

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amino acid sequence due to natural allelic variation or mutagenesis. Accordingly, a useful Tango-77 protein is a protein which includes an amino acid sequence at least about 45%, preferably 55%, 65%, 75%, 85%, 95%, or 99% identical to the amino acid sequence of SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13 and retains the functional activity of the Tango-77 proteins of SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13. In a preferred embodiment, the Tango-77 protein retains a functional activity of the Tango-77 protein of SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13.

To determine the percent identity of two amino acid sequences or of two nucleic acids, the sequences are aligned for optimal comparison purposes (e.g., gaps can be introduced in the sequence of a first amino acid or nucleic acid sequence for optimal alignment with a second amino or nucleic acid sequence). The amino acid residues or nucleotides at corresponding amino acid positions or nucleotide positions are then compared. When a position in the first sequence is occupied by the same amino acid residue or nucleotide as the corresponding position in the second sequence, then the molecules are identical at that position. The percent identity between the two sequences is a function of the number of identical positions shared by the sequences (i.e., % identity = # of identical positions/total # of positions, e.g., overlapping x 100). Preferably, the two sequences are the same length.

The determination of percent homology between two sequences can be accomplished using a mathematical algorithm. A preferred, non-limiting example of a mathematical algorithm utilized for the comparison of two sequences is the algorithm of Karlin and Altschul (1990)

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Proc. Natl. Acad. Sci. USA 87:2264-2268, modified as in Karlin and Altschul (1993) Proc. Natl. Acad. Sci. USA 90:5873-5877. Such an algorithm is incorporated into the NBLAST and XBLAST programs of Altschul, et al. (1990)

5 J. Mol. Biol. 215:403-410. BLAST nucleotide searches can be performed with the NBLAST program, score = 100, wordlength = 12 to obtain nucleotide sequences homologous to Tango-77 nucleic acid molecules of the invention. BLAST protein searches can be performed with the XBLAST

10 program, score = 50, wordlength = 3 to obtain amino acid sequences homologous to Tango-77 protein molecules of the invention. To obtain gapped alignments for comparison purposes, Gapped BLAST can be utilized as described in Altschul et al. (1997) Nucleic Acids Res. 25:3389-3402.

15 When utilizing BLAST and Gapped BLAST programs, the default parameters of the respective programs (e.g., XBLAST and NBLAST) can be used. See <http://www.ncbi.nlm.nih.gov>. Another preferred, non-limiting example of a mathematical algorithm utilized for

20 the comparison of sequences is the algorithm of Myers and Miller, CABIOS (1989). Such an algorithm is incorporated into the ALIGN program (version 2.0) which is part of the GCG sequence alignment software package. When utilizing the ALIGN program for comparing amino acid sequences, a

25 PAM120 weight residue table, a gap length penalty of 12, and a gap penalty of 4 can be used.

The percent identity between two sequences can be determined using techniques similar to those described above, with or without allowing gaps. In calculating

30 percent identity, only exact matches are counted.

The invention also provides Tango-77 chimeric or fusion proteins. As used herein, a Tango-77 "chimeric protein" or "fusion protein" comprises a Tango-77 polypeptide operably linked to a non-Tango-77

35 polypeptide. A "Tango-77 polypeptide" refers to a

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polypeptide having an amino acid sequence corresponding to Tango-77 polypeptides, whereas a "non-Tango-77 polypeptide" refers to a polypeptide having an amino acid sequence corresponding to a protein which is not substantially identical to the Tango-77 protein, e.g., a protein which is different from the Tango-77 protein and which is derived from the same or a different organism. Within a Tango-77 fusion protein the Tango-77 polypeptide can correspond to all or a portion of a Tango-77 protein, preferably at least one biologically active portion of a Tango-77 protein. Within the fusion protein, the term "operably linked" is intended to indicate that the Tango-77 polypeptide and the non-Tango-77 polypeptide are fused in-frame to each other. The non-Tango-77 polypeptide can be fused to the N-terminus or C-terminus of the Tango-77 polypeptide.

One useful fusion protein is a GST-Tango-77 fusion protein in which the Tango-77 sequences are fused to the C-terminus of the GST sequences. Such fusion proteins can facilitate the purification of recombinant Tango-77.

In another embodiment, the fusion protein is a Tango-77 protein containing a heterologous signal sequence at its N-terminus. For example, the native Tango-77 signal sequence (i.e., about amino acids 1 to 63 of SEQ ID NO:2; SEQ ID NO:4; or about amino acids 1 to 52 of SEQ ID NO:7; SEQ ID NO:8; or about amino acids 1 to 21 of SEQ ID NO:11; SEQ ID NO:12) can be removed and replaced with a signal sequence from another protein. In certain host cells (e.g., mammalian host cells), expression and/or secretion of Tango-77 can be increased through use of a heterologous signal sequence. For example, the gp67 secretory sequence of the baculovirus envelope protein can be used as a heterologous signal sequence (Ausubel et al., supra). Other examples of eukaryotic heterologous signal sequences include the secretory sequences of

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melittin and human placental alkaline phosphatase (Stratagene; La Jolla, California). In yet another example, useful prokaryotic heterologous signal sequences include the phoA secretory signal (Sambrook et al.,  
5 supra) and the protein A secretory signal (Pharmacia Biotech; Piscataway, New Jersey).

In yet another embodiment, the fusion protein is an Tango-77-immunoglobulin fusion protein in which all or part of Tango-77 is fused to sequences derived from a  
10 member of the immunoglobulin protein family. The Tango-77-immunoglobulin fusion proteins of the invention can be incorporated into pharmaceutical compositions and administered to a subject to inhibit an interaction between a Tango-77 ligand and a Tango-77 receptor on the  
15 surface of a cell, to thereby suppress Tango-77-mediated signal transduction in vivo. The Tango-77-immunoglobulin fusion proteins can be used to affect the bioavailability of a Tango-77 cognate ligand. Inhibition of the Tango-77 ligand/Tango-77 interaction may be useful therapeutically  
20 for both the treatment of inflammatory and autoimmune disorders. Moreover, the Tango-77-immunoglobulin fusion proteins of the invention can be used as immunogens to produce anti-Tango-77 antibodies in a subject, to purify Tango-77 ligands and in screening assays to identify  
25 molecules which inhibit the interaction of Tango-77 with a Tango-77 receptor.

Preferably, a Tango-77 chimeric or fusion protein of the invention is produced by standard recombinant DNA techniques. For example, DNA fragments coding for the  
30 different polypeptide sequences are ligated together in-frame in accordance with conventional techniques, for example by employing blunt-ended or stagger-ended termini for ligation, restriction enzyme digestion to provide for appropriate termini, filling-in of cohesive ends as  
35 appropriate, alkaline phosphatase treatment to avoid

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undesirable joining, and enzymatic ligation. In another embodiment, the fusion gene can be synthesized by conventional techniques including automated DNA synthesizers. Alternatively, PCR amplification of gene  
5 fragments can be carried out using anchor primers which give rise to complementary overhangs between two consecutive gene fragments which can subsequently be annealed and reamplified to generate a chimeric gene sequence (see, e.g., *Current Protocols in Molecular*  
10 *Biology*, Ausubel et al. eds., John Wiley & Sons: 1992). Moreover, many expression vectors are commercially available that already encode a fusion moiety (e.g., a GST polypeptide). An Tango-77-encoding nucleic acid can be cloned into such an expression vector such that the  
15 fusion moiety is linked in-frame to the Tango-77 protein.

The present invention also pertains to variants of the Tango-77 proteins (i.e., proteins having a sequence which differs from that of the Tango-77 amino acid sequence). Such variants can function as either Tango-77  
20 agonists (mimetics) or as Tango-77 antagonists. Variants of the Tango-77 protein can be generated by mutagenesis, e.g., discrete point mutation or truncation of the Tango-77 protein. An agonist of the Tango-77 protein can retain substantially the same, or a subset, of the  
25 biological activities of the naturally occurring form of the Tango-77 protein. An antagonist of the Tango-77 protein can inhibit one or more of the activities of the naturally occurring form of the Tango-77 protein by, for example, competitively binding to a downstream or  
30 upstream member of a cellular signaling cascade which includes the Tango-77 protein. Thus, specific biological effects can be elicited by treatment with a variant of limited function. Treatment of a subject with a variant having a subset of the biological activities of the  
35 naturally occurring form of the protein can have fewer

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side effects in a subject relative to treatment with the naturally occurring form of the Tango-77 proteins.

Variants of the Tango-77 protein which function as either Tango-77 agonists (mimetics) or as Tango-77  
5 antagonists can be identified by screening combinatorial libraries of mutants, e.g., truncation mutants, of the Tango-77 protein for Tango-77 protein agonist or antagonist activity. In one embodiment, a variegated library of Tango-77 variants is generated by  
10 combinatorial mutagenesis at the nucleic acid level and is encoded by a variegated gene library. A variegated library of Tango-77 variants can be produced by, for example, enzymatically ligating a mixture of synthetic oligonucleotides into gene sequences such that a  
15 degenerate set of potential Tango-77 sequences is expressible as individual polypeptides, or alternatively, as a set of larger fusion proteins (e.g., for phage display) containing the set of Tango-77 sequences therein. There are a variety of methods which can be  
20 used to produce libraries of potential Tango-77 variants from a degenerate oligonucleotide sequence. Chemical synthesis of a degenerate gene sequence can be performed in an automatic DNA synthesizer, and the synthetic gene then ligated into an appropriate expression vector. Use  
25 of a degenerate set of genes allows for the provision, in one mixture, of all of the sequences encoding the desired set of potential Tango-77 sequences. Methods for synthesizing degenerate oligonucleotides are known in the art (see, e.g., Narang (1983) *Tetrahedron* 39:3; Itakura  
30 et al. (1984) *Annu. Rev. Biochem.* 53:323; Itakura et al. (1984) *Science* 198:1056; Ike et al. (1983) *Nucleic Acid Res.* 11:477).

In addition, libraries of fragments of the Tango-77 protein coding sequence can be used to generate  
35 a variegated population of Tango-77 fragments for



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screening and subsequent selection of variants of a Tango-77 protein. In one embodiment, a library of coding sequence fragments can be generated by treating a double stranded PCR fragment of a Tango-77 coding sequence with  
5 a nuclease under conditions wherein nicking occurs only about once per molecule, denaturing the double stranded DNA, renaturing the DNA to form double stranded DNA which can include sense/antisense pairs from different nicked products, removing single stranded portions from reformed  
10 duplexes by treatment with S1 nuclease, and ligating the resulting fragment library into an expression vector. By this method, an expression library can be derived which encodes N-terminal and internal fragments of various sizes of the Tango-77 protein.

15 Several techniques are known in the art for screening gene products of combinatorial libraries made by point mutations or truncation, and for screening cDNA libraries for gene products having a selected property. Such techniques are adaptable for rapid screening of the  
20 gene libraries generated by the combinatorial mutagenesis of Tango-77 proteins. The most widely used techniques, which are amenable to high through-put analysis, for screening large gene libraries typically include cloning the gene library into replicable expression vectors,  
25 transforming appropriate cells with the resulting library of vectors, and expressing the combinatorial genes under conditions in which detection of a desired activity facilitates isolation of the vector encoding the gene whose product was detected. Recursive ensemble  
30 mutagenesis (REM), a technique which enhances the frequency of functional mutants in the libraries, can be used in combination with the screening assays to identify Tango-77 variants (Arkin and Yourvan (1992) *Proc. Natl. Acad. Sci. USA* 89:7811-7815; Delgrave et al. (1993)  
35 *Protein Engineering* 6(3):327-331).

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An isolated Tango-77 protein, or a portion or fragment thereof, can be used as an immunogen to generate antibodies that bind Tango-77 using standard techniques for polyclonal and monoclonal antibody preparation. The  
5 full-length Tango-77 protein can be used or, alternatively, the invention provides antigenic peptide fragments of Tango-77 for use as immunogens. The antigenic peptide of Tango-77 comprises at least 8 (preferably 10, 15, 20, or 30) amino acid residues of the  
10 amino acid sequence shown in SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11 or SEQ ID NO:13 and encompasses an epitope of Tango-77 such that an antibody raised against the peptide forms a specific immune complex with Tango-77.

15 A Tango-77 immunogen typically is used to prepare antibodies by immunizing a suitable subject (e.g., rabbit, goat, mouse or other mammal) with the immunogen. An appropriate immunogenic preparation can contain, for example, recombinantly expressed Tango-77 protein or a  
20 chemically synthesized Tango-77 polypeptide. The preparation can further include an adjuvant, such as Freund's complete or incomplete adjuvant, or similar immunostimulatory agent. Immunization of a suitable subject with an immunogenic Tango-77 preparation induces  
25 a polyclonal anti-Tango-77 antibody response.

Accordingly, another aspect of the invention pertains to anti-Tango-77 antibodies. The term "antibody" as used herein refers to immunoglobulin molecules and immunologically active portions of  
30 immunoglobulin molecules, i.e., molecules that contain an antigen binding site which specifically binds an antigen, such as Tango-77. A molecule which specifically binds to Tango-77 is a molecule which binds Tango-77, but does not substantially bind other molecules in a sample, e.g., a  
35 biological sample, which naturally contains Tango-77.

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Examples of immunologically active portions of immunoglobulin molecules include F(ab) and F(ab')<sub>2</sub> fragments which can be generated by treating the antibody with an enzyme such as pepsin. The invention provides polyclonal and monoclonal antibodies that bind Tango-77. The term "monoclonal antibody" or "monoclonal antibody composition", as used herein, refers to a population of antibody molecules that contain only one species of an antigen binding site capable of immunoreacting with a particular epitope of Tango-77. A monoclonal antibody composition thus typically displays a single binding affinity for a particular Tango-77 protein with which it immunoreacts.

Polyclonal anti-Tango-77 antibodies can be prepared as described above by immunizing a suitable subject with a Tango-77 immunogen. The anti-Tango-77 antibody titer in the immunized subject can be monitored over time by standard techniques, such as with an enzyme linked immunosorbent assay (ELISA) using immobilized Tango-77. If desired, the antibody molecules directed against Tango-77 can be isolated from the mammal (e.g., from the blood) and further purified by well-known techniques, such as protein A chromatography to obtain the IgG fraction. At an appropriate time after immunization, e.g., when the anti-Tango-77 antibody titers are highest, antibody-producing cells can be obtained from the subject and used to prepare monoclonal antibodies by standard techniques, such as the hybridoma technique originally described by Kohler and Milstein (1975) *Nature* 256:495-497, the human B cell hybridoma technique (Kozbor et al. (1983) *Immunol Today* 4:72), the EBV-hybridoma technique (Cole et al. (1985), *Monoclonal Antibodies and Cancer Therapy*, Alan R. Liss, Inc., pp. 77-96) or trioma techniques. The technology for producing hybridomas is well known (see generally Current

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Protocols in Immunology (1994) Coligan et al. (eds.) John Wiley & Sons, Inc., New York, NY). Briefly, an immortal cell line (typically a myeloma) is fused to lymphocytes (typically splenocytes) from a mammal immunized with a  
5 Tango-77 immunogen as described above, and the culture supernatants of the resulting hybridoma cells are screened to identify a hybridoma producing a monoclonal antibody that binds Tango-77.

Any of the many well known protocols used for  
10 fusing lymphocytes and immortalized cell lines can be applied for the purpose of generating an anti-Tango-77 monoclonal antibody (see, e.g., Current Protocols in Immunology, *supra*; Galfre et al. (1977) *Nature* 266:55052; R.H. Kenneth, in *Monoclonal Antibodies: A New Dimension*  
15 *In Biological Analyses*, Plenum Publishing Corp., New York, New York (1980); and Lerner (1981) *Yale J. Biol. Med.*, 54:387-402. Moreover, the ordinarily skilled worker will appreciate that there are many variations of such methods which also would be useful. Typically, the  
20 immortal cell line (e.g., a myeloma cell line) is derived from the same mammalian species as the lymphocytes. For example, murine hybridomas can be made by fusing lymphocytes from a mouse immunized with an immunogenic preparation of the present invention with an immortalized  
25 mouse cell line, e.g., a myeloma cell line that is sensitive to culture medium containing hypoxanthine, aminopterin and thymidine ("HAT medium"). Any of a number of myeloma cell lines can be used as a fusion partner according to standard techniques, e.g., the P3-  
30 NS1/1-Ag4-1, P3-x63-Ag8.653 or Sp2/O-Ag14 myeloma lines. These myeloma lines are available from ATCC. Typically, HAT-sensitive mouse myeloma cells are fused to mouse splenocytes using polyethylene glycol ("PEG"). Hybridoma cells resulting from the fusion are then selected using  
35 HAT medium, which kills unfused and unproductively fused

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myeloma cells (unfused splenocytes die after several days because they are not transformed). Hybridoma cells producing a monoclonal antibody of the invention are detected by screening the hybridoma culture supernatants  
5 for antibodies that bind Tango-77, e.g., using a standard ELISA assay.

Alternative to preparing monoclonal antibody-secreting hybridomas, a monoclonal anti-Tango-77 antibody can be identified and isolated by screening a recombinant  
10 combinatorial immunoglobulin library (e.g., an antibody phage display library) with Tango-77 to thereby isolate immunoglobulin library members that bind Tango-77. Kits for generating and screening phage display libraries are commercially available (e.g., the Pharmacia Recombinant  
15 Phage Antibody System, Catalog No. 27-9400-01; and the Stratagene SurfZAP™ Phage Display Kit, Catalog No. 240612). Additionally, examples of methods and reagents particularly amenable for use in generating and screening antibody display library can be found in, for example,  
20 U.S. Patent No. 5,223,409; PCT Publication No. WO 92/18619; PCT Publication No. WO 91/17271; PCT Publication No. WO 92/20791; PCT Publication No. WO 92/15679; PCT Publication No. WO 93/01288; PCT Publication No. WO 92/01047; PCT Publication No. WO  
25 92/09690; PCT Publication No. WO 90/02809; Fuchs et al. (1991) *Bio/Technology* 9:1370-1372; Hay et al. (1992) *Hum. Antibod. Hybridomas* 3:81-85; Huse et al. (1989) *Science* 246:1275-1281; Griffiths et al. (1993) *EMBO J* 12:725-734.

Additionally, recombinant anti-Tango-77  
30 antibodies, such as chimeric and humanized monoclonal antibodies, comprising both human and non-human portions, which can be made using standard recombinant DNA techniques, are within the scope of the invention. Such chimeric and humanized monoclonal antibodies can be  
35 produced by recombinant DNA techniques known in the art,

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for example using methods described in PCT Publication No. WO 87/02671; European Patent Application 184,187; European Patent Application 171,496; European Patent Application 173,494; PCT Publication No. WO 86/01533; 5 U.S. Patent No. 4,816,567; European Patent Application 125,023; Better et al. (1988) *Science* 240:1041-1043; Liu et al. (1987) *Proc. Natl. Acad. Sci. USA* 84:3439-3443; Liu et al. (1987) *J. Immunol.* 139:3521-3526; Sun et al. (1987) *Proc. Natl. Acad. Sci. USA* 84:214-218; Nishimura 10 et al. (1987) *Canc. Res.* 47:999-1005; Wood et al. (1985) *Nature* 314:446-449; and Shaw et al. (1988) *J. Natl. Cancer Inst.* 80:1553-1559; Morrison (1985) *Science* 229:1202-1207; Oi et al. (1986) *Bio/Techniques* 4:214; U.S. Patent 5,225,539; Jones et al. (1986) *Nature* 15 321:552-525; Verhoeyan et al. (1988) *Science* 239:1534; and Beidler et al. (1988) *J. Immunol.* 141:4053-4060.

Completely human antibodies are particularly desirable for therapeutic treatment of human patients. Such antibodies can be produced using transgenic mice 20 which are incapable of expressing endogenous immunoglobulin heavy and light chains genes, but which can express human heavy and light chain genes. The transgenic mice are immunized in the normal fashion with a selected antigen, e.g., all or a portion of Tango-77. 25 Monoclonal antibodies directed against the antigen can be obtained using conventional hybridoma technology. The human immunoglobulin transgenes harbored by the transgenic mice rearrange during B cell differentiation, and subsequently undergo class switching and somatic 30 mutation. Thus, using such a technique, it is possible to produce therapeutically useful IgG, IgA and IgE antibodies. For an overview of this technology for producing human antibodies, see Lonberg and Huszar (1995, *Int. Rev. Immunol.* 13:65-93). For a detailed discussion 35 of this technology for producing human antibodies and

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human monoclonal antibodies and protocols for producing such antibodies, see, e.g., U.S. Patent 5,625,126; U.S. Patent 5,633,425; U.S. Patent 5,569,825; U.S. Patent 5,661,016; and U.S. Patent 5,545,806. In addition, 5 companies such as Abgenix, Inc. (Freemont, CA), can be engaged to provide human antibodies directed against a selected antigen using technology similar to the described above.

Completely human antibodies which recognize a 10 selected epitope can be generated using a technique referred to as "guided selection." In this approach a selected non-human monoclonal antibody, e.g., a murine antibody, is used to guide the selection of a completely human antibody recognizing the same epitope.

15 First, a non-human monoclonal antibody which binds a selected antigen (epitope), e.g., an antibody which inhibits Tango-77 activity, is identified. The heavy chain and the light chain of the non-human antibody are cloned and used to create phage display Fab fragments. 20 For example, the heavy chain gene can be cloned into a plasmid vector so that the heavy chain can be secreted from bacteria. The light chain gene can be cloned into a phage coat protein gene so that the light chain can be expressed on the surface of phage. A repertoire (random 25 collection) of human light chains fused to phage is used to infect the bacteria which express the non-human heavy chain. The resulting progeny phage display hybrid antibodies (human light chain/non-human heavy chain). The selected antigen is used in a panning screen to 30 select phage which bind the selected antigen. Several rounds of selection may be required to identify such phage. Next, human light chain genes are isolated from the selected phage which bind the selected antigen. These selected human light chain genes are then used to 35 guide the selection of human heavy chain genes as

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follows. The selected human light chain genes are inserted into vectors for expression by bacteria. Bacteria expressing the selected human light chains are infected with a repertoire of human heavy chains fused to  
5 phage. The resulting progeny phage display human antibodies (human light chain/human heavy chain).

Next, the selected antigen is used in a panning screen to select phage which bind the selected antigen. The phage selected in this step display completely human  
10 antibody which recognize the same epitope recognized by the original selected, non-human monoclonal antibody. The genes encoding both the heavy and light chains are readily isolated and be further manipulated for production of human antibody. This technology is  
15 described by Jespers et al. (1994, *Bio/technology* 12:899-903).

An anti-Tango-77 antibody (e.g., monoclonal antibody) can be used to isolate Tango-77 by standard techniques, such as affinity chromatography or  
20 immunoprecipitation. An anti-Tango-77 antibody can facilitate the purification of natural Tango-77 from cells and of recombinantly produced Tango-77 expressed in host cells. Moreover, an anti-Tango-77 antibody can be used to detect Tango-77 protein (e.g., in a cellular  
25 lysate or cell supernatant) in order to evaluate the abundance and pattern of expression of the Tango-77 protein. Anti-Tango-77 antibodies can be used diagnostically to monitor protein levels in tissue as part of a clinical testing procedure, e.g., to, for  
30 example, determine the efficacy of a given treatment regimen. Detection can be facilitated by coupling the antibody to a detectable substance. Examples of detectable substances include various enzymes, prosthetic groups, fluorescent materials, luminescent materials,  
35 bioluminescent materials, and radioactive materials.



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Examples of suitable enzymes include horseradish peroxidase, alkaline phosphatase,  $\beta$ -galactosidase, or acetylcholinesterase; examples of suitable prosthetic group complexes include streptavidin/biotin and  
5 avidin/biotin; examples of suitable fluorescent materials include umbelliferone, fluorescein, fluorescein isothiocyanate, rhodamine, dichlorotriazinylamine fluorescein, dansyl chloride or phycoerythrin; an example of a luminescent material includes luminol; examples of  
10 bioluminescent materials include luciferase, luciferin, and aequorin, and examples of suitable radioactive material include  $^{125}\text{I}$ ,  $^{131}\text{I}$ ,  $^{35}\text{S}$  or  $^3\text{H}$ .

### III. Recombinant Expression Vectors and Host Cells

Another aspect of the invention pertains to  
15 vectors, preferably expression vectors, containing a nucleic acid molecule encoding Tango-77 (or a portion thereof). As used herein, the term "vector" refers to a nucleic acid molecule capable of transporting another nucleic acid to which it has been linked. One type of  
20 vector is a "plasmid", which refers to a circular double stranded DNA loop into which additional DNA segments can be ligated. Another type of vector is a viral vector, wherein additional DNA segments can be ligated into the viral genome. Certain vectors are capable of autonomous  
25 replication in a host cell into which they are introduced (e.g., bacterial vectors having a bacterial origin of replication and episomal mammalian vectors). Other vectors (e.g., non-episomal mammalian vectors) are integrated into the genome of a host cell upon  
30 introduction into the host cell, and thereby are replicated along with the host genome. Moreover, certain vectors, expression vectors, are capable of directing the expression of genes to which they are operably linked. In general, expression vectors of utility in recombinant

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DNA techniques are often in the form of plasmids (vectors). However, the invention is intended to include such other forms of expression vectors, such as viral vectors (e.g., replication defective retroviruses, adenoviruses and adeno-associated viruses), which serve equivalent functions.

The recombinant expression vectors of the invention comprise a nucleic acid of the invention in a form suitable for expression of the nucleic acid in a host cell, which means that the recombinant expression vectors include one or more regulatory sequences, selected on the basis of the host cells to be used for expression, which is operably linked to the nucleic acid sequence to be expressed. Within a recombinant expression vector, "operably linked" is intended to mean that the nucleotide sequence of interest is linked to the regulatory sequence(s) in a manner which allows for expression of the nucleotide sequence (e.g., in an *in vitro* transcription/translation system or in a host cell when the vector is introduced into the host cell). The term "regulatory sequence" is intended to include promoters, enhancers and other expression control elements (e.g., polyadenylation signals). Such regulatory sequences are described, for example, in Goeddel; *Gene Expression Technology: Methods in Enzymology* 185, Academic Press, San Diego, CA (1990). Regulatory sequences include those which direct constitutive expression of a nucleotide sequence in many types of host cell and those which direct expression of the nucleotide sequence only in certain host cells (e.g., tissue-specific regulatory sequences). It will be appreciated by those skilled in the art that the design of the expression vector can depend on such factors as the choice of the host cell to be transformed, the level of expression of protein desired, etc. The expression

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vectors of the invention can be introduced into host cells to thereby produce proteins or peptides, including fusion proteins or peptides, encoded by nucleic acids as described herein (e.g., Tango-77 proteins, mutant forms  
5 of Tango-77, fusion proteins, etc.).

The recombinant expression vectors of the invention can be designed for expression of Tango-77 in prokaryotic or eukaryotic cells, e.g., bacterial cells such as *E. coli*, insect cells (using baculovirus  
10 expression vectors), yeast cells or mammalian cells. Suitable host cells are discussed further in Goeddel, *Gene Expression Technology: Methods in Enzymology* 185, Academic Press, San Diego, CA (1990). Alternatively, the recombinant expression vector can be transcribed and  
15 translated *in vitro*, for example using T7 promoter regulatory sequences and T7 polymerase.

Expression of proteins in prokaryotes is most often carried out in *E. coli* with vectors containing constitutive or inducible promoters directing the  
20 expression of either fusion or non-fusion proteins. Fusion vectors add a number of amino acids to a protein encoded therein, usually to the amino terminus of the recombinant protein. Such fusion vectors typically serve three purposes: 1) to increase expression of recombinant  
25 protein; 2) to increase the solubility of the recombinant protein; and 3) to aid in the purification of the recombinant protein by acting as a ligand in affinity purification. Often, in fusion expression vectors, a proteolytic cleavage site is introduced at the junction  
30 of the fusion moiety and the recombinant protein to enable separation of the recombinant protein from the fusion moiety subsequent to purification of the fusion protein. Such enzymes, and their cognate recognition sequences, include Factor Xa, thrombin and enterokinase.  
35 Typical fusion expression vectors include pGEX (Pharmacia

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Biotech Inc; Smith and Johnson (1988) *Gene* 67:31-40),  
pMAL (New England Biolabs, Beverly, MA) and pRIT5  
(Pharmacia, Piscataway, NJ) which fuse glutathione S-  
transferase (GST), maltose E binding protein, or protein  
5 A, respectively, to the target recombinant protein.

Examples of suitable inducible non-fusion *E. coli*  
expression vectors include pTrc (Amann et al. (1988) *Gene*  
69:301-315) and pET 11d (Studier et al., *Gene Expression*  
*Technology: Methods in Enzymology* 185, Academic Press,  
10 San Diego, California (1990) 60-89). Target gene  
expression from the pTrc vector relies on host RNA  
polymerase transcription from a hybrid trp-lac fusion  
promoter. Target gene expression from the pET 11d vector  
relies on transcription from a T7 gn10-lac fusion  
15 promoter mediated by a coexpressed viral RNA polymerase  
(T7 gn1). This viral polymerase is supplied by host  
strains BL21(DE3) or HMS174(DE3) from a resident  $\lambda$   
prophage harboring a T7 gn1 gene under the  
transcriptional control of the lacUV 5 promoter.

20 One strategy to maximize recombinant protein  
expression in *E. coli* is to express the protein in a host  
bacteria with an impaired capacity to proteolytically  
cleave the recombinant protein (Gottesman, *Gene*  
*Expression Technology: Methods in Enzymology* 185,  
25 Academic Press, San Diego, California (1990) 119-128).  
Another strategy is to alter the nucleic acid sequence of  
the nucleic acid to be inserted into an expression vector  
so that the individual codons for each amino acid are  
those preferentially utilized in *E. coli* (Wada et al.  
30 (1992) *Nucleic Acids Res.* 20:2111-2118). Such alteration  
of nucleic acid sequences of the invention can be carried  
out by standard DNA synthesis techniques.

In another embodiment, the Tango-77 expression  
vector is a yeast expression vector. Examples of vectors  
35 for expression in yeast *S. cerevisiae* include pYepSec1

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(Baldari et al. (1987) *EMBO J.* 6:229-234), pMFa (Kurjan and Herskowitz (1982) *Cell* 30:933-943), pJRY88 (Schultz et al. (1987) *Gene* 54:113-123), pYES2 (Invitrogen Corporation, San Diego, CA), and picZ (Invitrogen Corp,  
5 San Diego, CA).

Alternatively, Tango-77 can be expressed in insect cells using baculovirus expression vectors. Baculovirus vectors available for expression of proteins in cultured insect cells (e.g., Sf 9 cells) include the pAc series  
10 (Smith et al. (1983) *Mol. Cell Biol.* 3:2156-2165) and the pVL series (Lucklow and Summers (1989) *Virology* 170:31-39).

In yet another embodiment, a nucleic acid of the invention is expressed in mammalian cells using a  
15 mammalian expression vector. Examples of mammalian expression vectors include pCDM8 (Seed (1987) *Nature* 329:840) and pMT2PC (Kaufman et al. (1987) *EMBO J.* 6:187-195). When used in mammalian cells, the expression vector's control functions are often provided by viral  
20 regulatory elements. For example, commonly used promoters are derived from polyoma, Adenovirus 2, cytomegalovirus and Simian Virus 40. For other suitable expression systems for both prokaryotic and eukaryotic cells see chapters 16 and 17 of Sambrook et al. (*supra*).

25 In another embodiment, the recombinant mammalian expression vector is capable of directing expression of the nucleic acid preferentially in a particular cell type (e.g., tissue-specific regulatory elements are used to express the nucleic acid). Tissue-specific regulatory  
30 elements are known in the art. Non-limiting examples of suitable tissue-specific promoters include the albumin promoter (liver-specific; Pinkert et al. (1987) *Genes Dev.* 1:268-277), lymphoid-specific promoters (Calame and Eaton (1988) *Adv. Immunol.* 43:235-275), in particular  
35 promoters of T cell receptors (Winoto and Baltimore

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(1989) *EMBO J.* 8:729-733) and immunoglobulins (Banerji et al. (1983) *Cell* 33:729-740; Queen and Baltimore (1983) *Cell* 33:741-748), neuron-specific promoters (e.g., the neurofilament promoter; Byrne and Ruddle (1989) *Proc. Natl. Acad. Sci. USA* 86:5473-5477), pancreas-specific promoters (Edlund et al. (1985) *Science* 230:912-916), and mammary gland-specific promoters (e.g., milk whey promoter; U.S. Patent No. 4,873,316 and European Application Publication No. 264,166). Developmentally-regulated promoters are also encompassed, for example the murine hox promoters (Kessel and Gruss (1990) *Science* 249:374-379) and the  $\alpha$ -fetoprotein promoter (Campes and Tilghman (1989) *Genes Dev.* 3:537-546).

The invention further provides a recombinant expression vector comprising a DNA molecule of the invention cloned into the expression vector in an antisense orientation. That is, the DNA molecule is operably linked to a regulatory sequence in a manner which allows for expression (by transcription of the DNA molecule) of an RNA molecule which is antisense to Tango-77 mRNA. Regulatory sequences operably linked to a nucleic acid cloned in the antisense orientation can be chosen which direct the continuous expression of the antisense RNA molecule in a variety of cell types, for instance viral promoters and/or enhancers, or regulatory sequences can be chosen which direct constitutive, tissue specific or cell type specific expression of antisense RNA. The antisense expression vector can be in the form of a recombinant plasmid, phagemid or attenuated virus in which antisense nucleic acids are produced under the control of a high efficiency regulatory region, the activity of which can be determined by the cell type into which the vector is introduced. For a discussion of the regulation of gene expression using antisense genes see

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Weintraub et al. (*Reviews - Trends in Genetics*, Vol. 1(1) 1986).

Another aspect of the invention pertains to host cells into which a recombinant expression vector of the invention has been introduced. The terms "host cell" and "recombinant host cell" are used interchangeably herein. It is understood that such terms refer not only to the particular subject cell but to the progeny or potential progeny of such a cell. Because certain modifications may occur in succeeding generations due to either mutation or environmental influences, such progeny may not, in fact, be identical to the parent cell, but are still included within the scope of the term as used herein.

A host cell can be any prokaryotic or eukaryotic cell. For example, Tango-77 protein can be expressed in bacterial cells such as *E. coli*, insect cells, yeast or mammalian cells (such as Chinese hamster ovary cells (CHO) or COS cells). Other suitable host cells are known to those skilled in the art.

Vector DNA can be introduced into prokaryotic or eukaryotic cells via conventional transformation or transfection techniques. As used herein, the terms "transformation" and "transfection" are intended to refer to a variety of art-recognized techniques for introducing foreign nucleic acid (e.g., DNA) into a host cell, including calcium phosphate or calcium chloride coprecipitation, DEAE-dextran-mediated transfection, lipofection, or electroporation. Suitable methods for transforming or transfecting host cells can be found in Sambrook, et al. (*supra*), and other laboratory manuals.

For stable transfection of mammalian cells, it is known that, depending upon the expression vector and transfection technique used, only a small fraction of cells may integrate the foreign DNA into their genome.

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In order to identify and select these integrants, a gene that encodes a selectable marker (e.g., for resistance to antibiotics) is generally introduced into the host cells along with the gene of interest. Preferred selectable  
5 markers include those which confer resistance to drugs, such as G418, hygromycin and methotrexate. Nucleic acid encoding a selectable marker can be introduced into a host cell on the same vector as that encoding Tango-77 or can be introduced on a separate vector. Cells stably  
10 transfected with the introduced nucleic acid can be identified by drug selection (e.g., cells that have incorporated the selectable marker gene will survive, while the other cells die).

A host cell of the invention, such as a  
15 prokaryotic or eukaryotic host cell in culture, can be used to produce (i.e., express) Tango-77 protein. Accordingly, the invention further provides methods for producing Tango-77 protein using the host cells of the invention. In one embodiment, the method comprises  
20 culturing the host cell of invention (into which a recombinant expression vector encoding Tango-77 has been introduced) in a suitable medium such that Tango-77 protein is produced. In another embodiment, the method further comprises isolating Tango-77 from the medium or  
25 the host cell.

The host cells of the invention can also be used to produce nonhuman transgenic animals. For example, in one embodiment, a host cell of the invention is a fertilized oocyte or an embryonic stem cell into which  
30 Tango-77-coding sequences have been introduced. Such host cells can then be used to create non-human transgenic animals in which exogenous Tango-77 sequences have been introduced into their genome or homologous recombinant animals in which endogenous Tango-77  
35 sequences have been altered. Such animals are useful for



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studying the function and/or activity of Tango-77 and for identifying and/or evaluating modulators of Tango-77 activity. As used herein, a "transgenic animal" is a non-human animal, preferably a mammal, more preferably a rodent such as a rat or mouse, in which one or more of the cells of the animal includes a transgene. Other examples of transgenic animals include non-human primates, sheep, dogs, cows, goats, chickens, amphibians, etc. A transgene is exogenous DNA which is integrated into the genome of a cell from which a transgenic animal develops and which remains in the genome of the mature animal, thereby directing the expression of an encoded gene product in one or more cell types or tissues of the transgenic animal. As used herein, an "homologous recombinant animal" is a non-human animal, preferably a mammal, more preferably a mouse, in which an endogenous Tango-77 gene has been altered by homologous recombination between the endogenous gene and an exogenous DNA molecule introduced into a cell of the animal, e.g., an embryonic cell of the animal, prior to development of the animal.

A transgenic animal of the invention can be created by introducing Tango-77-encoding nucleic acid into the male pronuclei of a fertilized oocyte, e.g., by microinjection, retroviral infection, and allowing the oocyte to develop in a pseudopregnant female foster animal. The Tango-77 cDNA sequence e.g., that of (SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6; SEQ ID NO:10 or the cDNA of ATCC 98807) can be introduced as a transgene into the genome of a non-human animal. Alternatively, a nonhuman homologue of the human Tango-77 gene, such as a mouse Tango-77 gene, can be isolated based on hybridization to the human Tango-77 cDNA and used as a transgene.

Intronic sequences and polyadenylation signals can also be included in the transgene to increase the efficiency

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of expression of the transgene. A tissue-specific regulatory sequence(s) can be operably linked to the Tango-77 transgene to direct expression of Tango-77 protein to particular cells. Methods for generating transgenic animals via embryo manipulation and microinjection, particularly animals such as mice, have become conventional in the art and are described, for example, in U.S. Patent Nos. 4,736,866 and 4,870,009, U.S. Patent No. 4,873,191 and in Hogan, *Manipulating the Mouse Embryo* (Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y., 1986). Similar methods are used for production of other transgenic animals. A transgenic founder animal can be identified based upon the presence of the Tango-77 transgene in its genome and/or expression of Tango-77 mRNA in tissues or cells of the animals. A transgenic founder animal can then be used to breed additional animals carrying the transgene. Moreover, transgenic animals carrying a transgene encoding Tango-77 can further be bred to other transgenic animals carrying other transgenes.

To create an homologous recombinant animal, a vector is prepared which contains at least a portion of a Tango-77 gene (e.g., a human or a non-human homolog of the Tango-77 gene, e.g., a murine Tango-77 gene) into which a deletion, addition or substitution has been introduced to thereby alter, e.g., functionally disrupt, the Tango-77 gene. In a preferred embodiment, the vector is designed such that, upon homologous recombination, the endogenous Tango-77 gene is functionally disrupted (i.e., no longer encodes a functional protein; also referred to as a "knock out" vector). Alternatively, the vector can be designed such that, upon homologous recombination, the endogenous Tango-77 gene is mutated or otherwise altered but still encodes functional protein (e.g., the upstream regulatory region can be altered to thereby

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alter the expression of the endogenous Tango-77 protein). In the homologous recombination vector, the altered portion of the Tango-77 gene is flanked at its 5' and 3' ends by additional nucleic acid of the Tango-77 gene to  
5 allow for homologous recombination to occur between the exogenous Tango-77 gene carried by the vector and an endogenous Tango-77 gene in an embryonic stem cell. The additional flanking Tango-77 nucleic acid is of sufficient length for successful homologous recombination  
10 with the endogenous gene. Typically, several kilobases of flanking DNA (both at the 5' and 3' ends) are included in the vector (see, e.g., Thomas and Capecchi (1987) *Cell* 51:503 for a description of homologous recombination vectors). The vector is introduced into an embryonic  
15 stem cell line (e.g., by electroporation) and cells in which the introduced Tango-77 gene has homologously recombined with the endogenous Tango-77 gene are selected (see, e.g., Li et al. (1992) *Cell* 69:915). The selected cells are then injected into a blastocyst of an animal  
20 (e.g., a mouse) to form aggregation chimeras (see, e.g., Bradley in *Teratocarcinomas and Embryonic Stem Cells: A Practical Approach*, Robertson, ed. (IRL, Oxford, 1987) pp. 113-152). A chimeric embryo can then be implanted into a suitable pseudopregnant female foster animal and  
25 the embryo brought to term. Progeny harboring the homologously recombined DNA in their germ cells can be used to breed animals in which all cells of the animal contain the homologously recombined DNA by germline transmission of the transgene. Methods for constructing  
30 homologous recombination vectors and homologous recombinant animals are described further in Bradley (1991) *Current Opinion in Bio/Technology* 2:823-829 and in PCT Publication Nos. WO 90/11354, WO 91/01140, WO 92/0968, and WO 93/04169.

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In another embodiment, transgenic non-human animals can be produced which contain selected systems which allow for regulated expression of the transgene. One example of such a system is the *cre/loxP* recombinase system of bacteriophage P1. For a description of the *cre/loxP* recombinase system, see, e.g., Lakso et al. (1992) *Proc. Natl. Acad. Sci. USA* 89:6232-6236. Another example of a recombinase system is the FLP recombinase system of *Saccharomyces cerevisiae* (O'Gorman et al. (1991) *Science* 251:1351-1355. If a *cre/loxP* recombinase system is used to regulate expression of the transgene, animals containing transgenes encoding both the Cre recombinase and a selected protein are required. Such animals can be provided through the construction of "double" transgenic animals, e.g., by mating two transgenic animals, one containing a transgene encoding a selected protein and the other containing a transgene encoding a recombinase.

Clones of the non-human transgenic animals described herein can also be produced according to the methods described in Wilmut et al. (1997) *Nature* 385:810-813 and PCT Publication Nos. WO 97/07668 and WO 97/07669. In brief, a cell, e.g., a somatic cell, from the transgenic animal can be isolated and induced to exit the growth cycle and enter G<sub>0</sub> phase. The quiescent cell can then be fused, e.g., through the use of electrical pulses, to an enucleated oocyte from an animal of the same species from which the quiescent cell is isolated. The reconstructed oocyte is then cultured such that it develops to morula or blastocyte and then transferred to pseudopregnant female foster animal. The offspring borne of this female foster animal will be a clone of the animal from which the cell, e.g., the somatic cell, is isolated.

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#### IV. Pharmaceutical Compositions

The Tango-77 nucleic acid molecules, Tango-77 proteins, and anti-Tango-77 antibodies (also referred to herein as "active compounds") of the invention can be  
5 incorporated into pharmaceutical compositions suitable for administration. Such compositions typically comprise the nucleic acid molecule, protein, or antibody and a pharmaceutically acceptable carrier. As used herein the language "pharmaceutically acceptable carrier" is  
10 intended to include any and all solvents, dispersion media, coatings, antibacterial and antifungal agents, isotonic and absorption delaying agents, and the like, compatible with pharmaceutical administration. The use of such media and agents for pharmaceutically active  
15 substances is well known in the art. Except insofar as any conventional media or agent is incompatible with the active compound, use thereof in the compositions is contemplated. Supplementary active compounds can also be incorporated into the compositions.

20 A pharmaceutical composition of the invention is formulated to be compatible with its intended route of administration. Examples of routes of administration include parenteral, (e.g. intravenous, intradermal, subcutaneous) (e.g., oral inhalation), transdermal  
25 (topical), transmucosal, and rectal administration. Solutions or suspensions used for parenteral, intradermal, or subcutaneous application can include the following components: a sterile diluent such as water for injection, saline solution, fixed oils, polyethylene  
30 glycols, glycerine, propylene glycol or other synthetic solvents; antibacterial agents such as benzyl alcohol or methyl parabens; antioxidants such as ascorbic acid or sodium bisulfite; chelating agents such as ethylenediaminetetraacetic acid; buffers such as  
35 acetates, citrates or phosphates and agents for the

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adjustment of tonicity such as sodium chloride or dextrose. pH can be adjusted with acids or bases, such as hydrochloric acid or sodium hydroxide. The parenteral preparation can be enclosed in ampoules, disposable  
5 syringes or multiple dose vials made of glass or plastic.

Pharmaceutical compositions suitable for injectable use include sterile aqueous solutions (where water soluble) or dispersions and sterile powders for the extemporaneous preparation of sterile injectable  
10 solutions or dispersions. For intravenous administration, suitable carriers include physiological saline, bacteriostatic water, Cremophor EL™ (BASF; Parsippany, NJ) or phosphate buffered saline (PBS). In all cases, the composition must be sterile and should be  
15 fluid to the extent that easy syringability exists. It must be stable under the conditions of manufacture and storage and must be preserved against the contaminating action of microorganisms such as bacteria and fungi. The carrier can be a solvent or dispersion medium containing,  
20 for example, water, ethanol, polyol (for example, glycerol, propylene glycol, and liquid polyethylene glycol, and the like), and suitable mixtures thereof. The proper fluidity can be maintained, for example, by the use of a coating such as lecithin, by the maintenance  
25 of the required particle size in the case of dispersion and by the use of surfactants. Prevention of the action of microorganisms can be achieved by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, ascorbic acid,  
30 thimerosal, and the like. In many cases, it will be preferable to include isotonic agents, for example, sugars, polyalcohols such as mannitol, sorbitol, sodium chloride in the composition. Prolonged absorption of the injectable compositions can be brought about by including

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in the composition an agent which delays absorption, for example, aluminum monostearate and gelatin.

Sterile injectable solutions can be prepared by incorporating the active compound (e.g., a Tango-77 protein or anti-Tango-77 antibody) in the required amount in an appropriate solvent with one or a combination of ingredients enumerated above, as required, followed by filtered sterilization. Generally, dispersions are prepared by incorporating the active compound into a sterile vehicle which contains a basic dispersion medium and the required other ingredients from those enumerated above. In the case of sterile powders for the preparation of sterile injectable solutions, the preferred methods of preparation are vacuum drying and freeze-drying which yields a powder of the active ingredient plus any additional desired ingredient from a previously sterile-filtered solution thereof.

Oral compositions generally include an inert diluent or an edible carrier. They can be enclosed in gelatin capsules or compressed into tablets. For the purpose of oral therapeutic administration, the active compound can be incorporated with excipients and used in the form of tablets, troches, or capsules. Oral compositions can also be prepared using a fluid carrier for use as a mouthwash, wherein the compound in the fluid carrier is applied orally and swished and expectorated or swallowed. Pharmaceutically compatible binding agents, and/or adjuvant materials can be included as part of the composition. The tablets, pills, capsules, troches and the like can contain any of the following ingredients, or compounds of a similar nature: a binder such as microcrystalline cellulose, gum tragacanth or gelatin; an excipient such as starch or lactose, a disintegrating agent such as alginic acid, Primogel, or corn starch; a lubricant such as magnesium stearate or Sterotes; a

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glidant such as colloidal silicon dioxide; a sweetening agent such as sucrose or saccharin; or a flavoring agent such as peppermint, methyl salicylate, or orange flavoring.

5           For administration by inhalation, the compounds are delivered in the form of an aerosol spray from a pressurized container or dispenser which contains a suitable propellant, e.g., a gas such as carbon dioxide, or a nebulizer.

10           Systemic administration can also be by transmucosal or transdermal means. For transmucosal or transdermal administration, penetrants appropriate to the barrier to be permeated are used in the formulation. Such penetrants are generally known in the art, and  
15 include, for example, for transmucosal administration, detergents, bile salts, and fusidic acid derivatives. Transmucosal administration can be accomplished through the use of nasal sprays or suppositories. For transdermal administration, the active compounds are  
20 formulated into ointments, salves, gels, or creams as generally known in the art.

          The compounds can also be prepared in the form of suppositories (e.g., with conventional suppository bases such as cocoa butter and other glycerides) or retention  
25 enemas for rectal delivery.

          In one embodiment, the active compounds are prepared with carriers that will protect the compound against rapid elimination from the body, such as a controlled release formulation, including implants and  
30 microencapsulated delivery systems. Biodegradable, biocompatible polymers can be used, such as ethylene vinyl acetate, polyanhydrides, polyglycolic acid, collagen, polyorthoesters, and polylactic acid. Methods for preparation of such formulations will be apparent to  
35 those skilled in the art. The materials can also be



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obtained commercially from Alza Corporation and Nova Pharmaceuticals, Inc. Liposomal suspensions (including liposomes targeted to infected cells with monoclonal antibodies to viral antigens) can also be used as  
5 pharmaceutically acceptable carriers. These can be prepared according to methods known to those skilled in the art, for example, as described in U.S. Patent No. 4,522,811.

It is especially advantageous to formulate oral or  
10 parenteral compositions in dosage unit form for ease of administration and uniformity of dosage. Dosage unit form as used herein refers to physically discrete units suited as unitary dosages for the subject to be treated; each unit containing a predetermined quantity of active  
15 compound calculated to produce the desired therapeutic effect in association with the required pharmaceutical carrier. The specification for the dosage unit forms of the invention are dictated by and directly dependent on the unique characteristics of the active compound and the  
20 particular therapeutic effect to be achieved, and the limitations inherent in the art of compounding such an active compound for the treatment of individuals.

The nucleic acid molecules of the invention can be inserted into vectors and used as gene therapy vectors.  
25 Gene therapy vectors can be delivered to a subject by, for example, intravenous injection, local administration (U.S. Patent 5,328,470) or by stereotactic injection (see, e.g., Chen et al. (1994) *Proc. Natl. Acad. Sci. USA* 91:3054-3057). The pharmaceutical preparation of the  
30 gene therapy vector can include the gene therapy vector in an acceptable diluent, or can comprise a slow release matrix in which the gene delivery vehicle is imbedded. Alternatively, where the complete gene delivery vector can be produced intact from recombinant cells, e.g.  
35 retroviral vectors, the pharmaceutical preparation can

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include one or more cells which produce the gene delivery system.

The pharmaceutical compositions can be included in a container, pack, or dispenser together with  
5 instructions for administration.

#### V. Uses and Methods of the Invention

The nucleic acid molecules, proteins, protein homologues, and antibodies described herein can be used in one or more of the following methods: a) screening  
10 assays; b) detection assays (e.g., chromosomal mapping, tissue typing, forensic biology); c) predictive medicine (e.g., diagnostic assays, prognostic assays, monitoring clinical trials, and pharmacogenomics); and d) methods of treatment (e.g., therapeutic and prophylactic). A  
15 Tango-77 protein interacts with other cellular proteins and can thus be used for regulation of inflammation. The polypeptides of the invention can be used in assays to determine biological activity. For example, they could be used in a panel of proteins for high-throughput  
20 screening.

The isolated nucleic acid molecules of the invention can be used to express Tango-77 protein (e.g., via a recombinant expression vector in a host cell in gene therapy applications), to detect Tango-77 mRNA  
25 (e.g., in a biological sample) or a genetic lesion in a Tango-77 gene, and to modulate Tango-77 activity. In addition, the Tango-77 proteins can be used to screen drugs or compounds which modulate the Tango-77 activity or expression as well as to treat disorders characterized  
30 by insufficient or excessive production of Tango-77 protein or production of Tango-77 protein forms which have decreased or aberrant activity compared to Tango-77 wild type protein. In addition, the anti-Tango-77

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antibodies of the invention can be used to detect and isolate Tango-77 proteins and modulate Tango-77 activity.

This invention further pertains to novel agents identified by the above-described screening assays and  
5 uses thereof for treatments as described herein.

#### A. Screening Assays

The invention provides a method (also referred to herein as a "screening assay") for identifying modulators, i.e., candidate or test compounds or agents  
10 (e.g., peptides, peptidomimetics, small molecules or other drugs) which bind to Tango-77 proteins or have a stimulatory or inhibitory effect on, for example, Tango-77 expression or Tango-77 activity.

Examples of methods for the synthesis of molecular  
15 libraries can be found in the art, for example in:  
DeWitt et al. (1993) *Proc. Natl. Acad. Sci. USA* 90:6909;  
Erb et al. (1994) *Proc. Natl. Acad. Sci. USA* 91:11422;  
Zuckermann et al. (1994). *J. Med. Chem.* 37:2678; Cho et al. (1993) *Science* 261:1303; Carrell et al. (1994) *Angew. Chem. Int. Ed. Engl.* 33:2059; Carrell et al. (1994) *Angew. Chem. Int. Ed. Engl.* 33:2061; and Gallop et al. (1994) *J. Med. Chem.* 37:1233.  
20

Libraries of compounds may be presented in solution (e.g., Houghten (1992) *Bio/Techniques* 13:412-  
25 421), or on beads (Lam (1991) *Nature* 354:82-84), chips (Fodor (1993) *Nature* 364:555-556), bacteria (U.S. Patent No. 5,223,409), spores (Patent Nos. 5,571,698; 5,403,484; and 5,223,409), plasmids (Cull et al. (1992) *Proc. Natl. Acad. Sci. USA* 89:1865-1869) or phage (Scott and Smith  
30 (1990) *Science* 249:386-390; Devlin (1990) *Science* 249:404-406; Cwirla et al. (1990) *Proc. Natl. Acad. Sci. USA* 87:6378-6382; and Felici (1991) *J. Mol. Biol.* 222:301-310).

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In another embodiment, an assay is used to determine the ability of the test compound to modulate the activity of Tango-77 or a biologically active portion thereof, for example, by determining the ability of the Tango-77 protein to bind to or interact with a Tango-77 target molecule. As used herein, a "target molecule" is a molecule with which a Tango-77 protein binds or interacts in nature, for example, a molecule on the surface of a cell. A Tango-77 target molecule can be a non-Tango-77 molecule or a Tango-77 protein or polypeptide of the present invention. In one embodiment, a Tango-77 target molecule is a component of a signal transduction pathway, for example, Tango-77 may bind to a IL-1 receptor or another receptor thereby blocking the receptor and inhibiting future signal transduction. Determining the ability of the Tango-77 protein to bind to or interact with a Tango-77 target molecule can be accomplished by one of the methods described above. In a preferred embodiment, determining the ability of the Tango-77 protein to bind to or interact with a Tango-77 target molecule can be accomplished by determining the activity of the target molecule. For example, the activity of the target molecule can be determined by detecting induction of a cellular second messenger of the target (e.g., intracellular  $\text{Ca}^{2+}$ , diacylglycerol, IP3, etc.), detecting catalytic/enzymatic activity of the target on an appropriate substrate, detecting the induction of a reporter gene (e.g., a Tango-77-responsive regulatory element operably linked to a nucleic acid encoding a detectable marker, e.g. luciferase), or detecting a cellular response, for example, inflammation.

In yet another embodiment, an assay of the present invention is a cell-free assay comprising contacting a Tango-77 protein or biologically active portion thereof with a test compound and determining the ability of the

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test compound to bind to the Tango-77 protein or biologically active portion thereof. Binding of the test compound to the Tango-77 protein can be determined either directly or indirectly as described above. In a preferred embodiment, the assay includes contacting the Tango-77 protein or biologically active portion thereof with a known compound which binds Tango-77 to form an assay mixture, contacting the assay mixture with a test compound, and determining the ability of the test compound to interact with a Tango-77 protein, wherein determining the ability of the test compound to interact with a Tango-77 protein comprises determining the ability of the test compound to preferentially bind to Tango-77 or biologically active portion thereof as compared to the known compound.

In another embodiment, an assay is a cell-free assay comprising contacting Tango-77 protein or biologically active portion thereof with a test compound and determining the ability of the test compound to modulate (e.g., stimulate or inhibit) the activity of the Tango-77 protein or biologically active portion thereof. Determining the ability of the test compound to modulate the activity of Tango-77 can be accomplished, for example, by determining the ability of the Tango-77 protein to bind to a Tango-77 target molecule by one of the methods described above for determining direct binding. In an alternative embodiment, determining the ability of the test compound to modulate the activity of Tango-77 can be accomplished by determining the ability of the Tango-77 protein to further modulate a Tango-77 target molecule. For example, the catalytic/enzymatic activity of the target molecule on an appropriate substrate can be determined as previously described.

In yet another embodiment, the cell-free assay comprises contacting the Tango-77 protein or biologically

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active portion thereof with a known compound which binds Tango-77 to form an assay mixture, contacting the assay mixture with a test compound, and determining the ability of the test compound to interact with a Tango-77 protein, wherein determining the ability of the test compound to interact with a Tango-77 protein comprises determining the ability of the Tango-77 protein to preferentially bind to or modulate the activity of a Tango-77 target molecule.

It is possible that membrane-bound forms of Tango-77 exist. The cell-free assays of the present invention are amenable to use of both the forms Tango-77. In the case of cell-free assays comprising a membrane-bound form of Tango-77, it may be desirable to utilize a solubilizing agent such that the membrane-bound form of Tango-77 is maintained in solution. Examples of such solubilizing agents include non-ionic detergents such as n-octylglucoside, n-dodecylglucoside, n-dodecylmaltoside, octanoyl-N-methylglucamide, decanoyl-N-methylglucamide, Triton® X-100, Triton® X-114, Thesit®, Isotridecypoly(ethylene glycol ether)n, 3-[(3-cholamidopropyl)dimethylamminio]-1-propane sulfonate (CHAPS), 3-[(3-cholamidopropyl)dimethylamminio]-2-hydroxy-1-propane sulfonate (CHAPSO), or N-dodecyl=N,N-dimethyl-3-ammonio-1-propane sulfonate.

In more than one embodiment of the above assay methods of the present invention, it may be desirable to immobilize either Tango-77 or its target molecule to facilitate separation of complexed from uncomplexed forms of one or both of the proteins, as well as to accommodate automation of the assay. Binding of a test compound to Tango-77, or interaction of Tango-77 with a target molecule in the presence and absence of a candidate compound, can be accomplished in any vessel suitable for containing the reactants. Examples of such vessels

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include microtitre plates, test tubes, and micro-centrifuge tubes. In one embodiment, a fusion protein can be provided which adds a domain that allows one or both of the proteins to be bound to a matrix. For  
5 example, glutathione-S-transferase/ Tango-77 fusion proteins or glutathione-S-transferase/target fusion proteins can be adsorbed onto glutathione sepharose beads (Sigma Chemical Co.; St. Louis, MO) or glutathione derivatized microtitre plates, which are then combined  
10 with the test compound or the test compound and either the non-adsorbed target protein or Tango-77 protein, and the mixture incubated under conditions conducive to complex formation (e.g., at physiological conditions for salt and pH). Following incubation, the beads or  
15 microtitre plate wells are washed to remove any unbound components and complex formation is measured either directly or indirectly, for example, as described above. Alternatively, the complexes can be dissociated from the matrix, and the level of Tango-77 binding or activity  
20 determined using standard techniques.

Other techniques for immobilizing proteins on matrices can also be used in the screening assays of the invention. For example, either Tango-77 or its target molecule can be immobilized utilizing conjugation of  
25 biotin and streptavidin. Biotinylated Tango-77 or target molecules can be prepared from biotin-NHS (N-hydroxy-succinimide) using techniques well known in the art (e.g., biotinylation kit, Pierce Chemicals; Rockford, IL), and immobilized in the wells of streptavidin-coated  
30 96 well plates (Pierce Chemical). Alternatively, antibodies reactive with Tango-77 or target molecules but which do not interfere with binding of the Tango-77 protein to its target molecule can be derivatized to the wells of the plate, and unbound target or Tango-77  
35 trapped in the wells by antibody conjugation. Methods

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for detecting such complexes, in addition to those described above for the GST-immobilized complexes, include immunodetection of complexes using antibodies reactive with the Tango-77 or target molecule, as well as  
5 enzyme-linked assays which rely on detecting an enzymatic activity associated with the Tango-77 or target molecule.

In another embodiment, modulators of Tango-77 expression are identified in a method in which a cell is contacted with a candidate compound and the expression of  
10 Tango-77 mRNA or protein in the cell is determined. The level of expression of Tango-77 mRNA or protein in the presence of the candidate compound is compared to the level of expression of Tango-77 mRNA or protein in the absence of the candidate compound. The candidate  
15 compound can then be identified as a modulator of Tango-77 expression based on this comparison. For example, when expression of Tango-77 mRNA or protein is greater (statistically significantly greater) in the presence of the candidate compound than in its absence,  
20 the candidate compound is identified as a stimulator of Tango-77 mRNA or protein expression. Alternatively, when expression of Tango-77 mRNA or protein is less (statistically significantly less) in the presence of the candidate compound than in its absence, the candidate  
25 compound is identified as an inhibitor of Tango-77 mRNA or protein expression. The level of Tango-77 mRNA or protein expression in the cells can be determined by methods described herein for detecting Tango-77 mRNA or protein.

30 In yet another aspect of the invention, the Tango-77 proteins can be used as "bait proteins" in a two-hybrid assay or three hybrid assay (see, e.g., U.S. Patent No. 5,283,317; Zervos et al. (1993) *Cell* 72:223-232; Madura et al. (1993) *J. Biol. Chem.* 268:12046-12054;  
35 Bartel et al. (1993) *Bio/Techniques* 14:920-924; Iwabuchi



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et al. (1993) *Oncogene* 8:1693-1696; and PCT Publication No. WO 94/10300), to identify other proteins, which bind to or interact with Tango-77 ("Tango-77-binding proteins" or "Tango-77-bp") and modulate Tango-77 activity. Such  
5 Tango-77-binding proteins are also likely to be involved in the propagation of signals by the Tango-77 proteins as, for example, upstream or downstream elements of the Tango-77 pathway.

The two-hybrid system is based on the modular  
10 nature of most transcription factors, which consist of separable DNA-binding and activation domains. Briefly, the assay utilizes two different DNA constructs. In one construct, the gene that codes for Tango-77 is fused to a gene encoding the DNA binding domain of a known  
15 transcription factor (e.g., GAL-4). In the other construct, a DNA sequence, from a library of DNA sequences, that encodes an unidentified protein ("prey" or "sample") is fused to a gene that codes for the activation domain of the known transcription factor. If  
20 the "bait" and the "prey" proteins are able to interact, in vivo, forming an Tango-77-dependent complex, the DNA-binding and activation domains of the transcription factor are brought into close proximity. This proximity allows transcription of a reporter gene (e.g., LacZ)  
25 which is operably linked to a transcriptional regulatory site responsive to the transcription factor. Expression of the reporter gene can be detected and cell colonies containing the functional transcription factor can be isolated and used to obtain the cloned gene which encodes  
30 the protein which interacts with Tango-77.

This invention further pertains to novel agents identified by the above-described screening assays and uses thereof for treatments as described herein.

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## B. Detection Assays

Portions or fragments of the cDNA sequence identified herein (and the corresponding complete gene sequences) can be used in numerous ways as polynucleotide reagents. For example, the sequence can be used to: (i) map the respective gene on a chromosome and, thus, locate gene regions associated with genetic disease; (ii) identify an individual from a minute biological sample (tissue typing); and (iii) aid in forensic identification of a biological sample. These applications are described in the subsections below.

### 1. Chromosome Mapping

Once the sequence (or a portion of the sequence) of a gene has been isolated, this sequence can be used to map the location of the gene on a chromosome. Accordingly, Tango-77 nucleic acid molecules described herein or fragments thereof, can be used to map the location of the Tango-77 gene(s) on a chromosome. The mapping of the Tango-77 sequences to chromosomes is an important first step in correlating these sequences with genes associated with disease.

Briefly, a Tango-77 gene can be mapped to chromosomes by preparing PCR primers (preferably 15-25 bp in length) from the Tango-77 sequences. Computer analysis of Tango-77 sequences can be used to rapidly select primers that do not span more than one exon in the genomic DNA, thus complicating the amplification process. These primers can then be used for PCR screening of somatic cell hybrids containing individual human chromosomes. Only those hybrids containing the human gene corresponding to the Tango-77 sequences will yield an amplified fragment.

Somatic cell hybrids are prepared by fusing somatic cells from different mammals (e.g., human and

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mouse cells). As hybrids of human and mouse cells grow and divide, they gradually lose human chromosomes in random order, but retain the mouse chromosomes. By using media in which mouse cells cannot grow (because they lack a particular enzyme) but in which human cells can, the one human chromosome that contains the gene encoding the needed enzyme, will be retained. By using various media, panels of hybrid cell lines can be established. Each cell line in a panel contains either a single human chromosome or a small number of human chromosomes, and a full set of mouse chromosomes, allowing easy mapping of individual genes to specific human chromosomes. (D'Eustachio et al. (1983) *Science* 220:919-924). Somatic cell hybrids containing only fragments of human chromosomes can also be produced by using human chromosomes with translocations and deletions.

PCR mapping of somatic cell hybrids is a rapid procedure for assigning a particular sequence to a particular chromosome. Three or more sequences can be assigned per day using a single thermal cycler. Using the Tango-77 sequences to design oligonucleotide primers, sublocalization can be achieved with panels of fragments from specific chromosomes. Other mapping strategies which can similarly be used to map a Tango-77 sequence to its chromosome include *in situ* hybridization (described in Fan et al. (1990) *Proc. Natl. Acad. Sci. USA* 87:6223-27), pre-screening with labeled flow-sorted chromosomes, and pre-selection by hybridization to chromosome specific cDNA libraries.

Fluorescence *in situ* hybridization (FISH) of a DNA sequence to a metaphase chromosomal spread can further be used to provide a precise chromosomal location in one step. Chromosome spreads can be made using cells whose division has been blocked in metaphase by a chemical, e.g., colcemid that disrupts the mitotic spindle. The

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chromosomes can be treated briefly with trypsin, and then stained with Giemsa. A pattern of light and dark bands develops on each chromosome, so that the chromosomes can be identified individually. The FISH technique can be  
5 used with a DNA sequence as short as 500 or 600 bases. However, clones larger than 1,000 bases have a higher likelihood of binding to a unique chromosomal location with sufficient signal intensity for simple detection. Preferably 1,000 bases, and more preferably 2,000 bases  
10 will suffice to get good results at a reasonable amount of time. For a review of this technique, see Verma et al. (Human Chromosomes: A Manual of Basic Techniques (Pergamon Press, New York, 1988)).

Reagents for chromosome mapping can be used  
15 individually to mark a single chromosome or a single site on that chromosome, or panels of reagents can be used for marking multiple sites and/or multiple chromosomes. Reagents corresponding to noncoding regions of the genes actually are preferred for mapping purposes. Coding  
20 sequences are more likely to be conserved within gene families, thus increasing the chance of cross hybridizations during chromosomal mapping.

Once a sequence has been mapped to a precise chromosomal location, the physical position of the  
25 sequence on the chromosome can be correlated with genetic map data. (Such data are found, for example, in V. McKusick, Mendelian Inheritance in Man, available on-line through Johns Hopkins University Welch Medical Library). The relationship between genes and disease, mapped to the  
30 same chromosomal region, can then be identified through linkage analysis (co-inheritance of physically adjacent genes), described in, e.g., Egeland et al. (1987) Nature 325:783-787.

Moreover, differences in the DNA sequences between  
35 individuals affected and unaffected with a disease

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associated with the Tango-77 gene can be determined. If a mutation is observed in some or all of the affected individuals but not in any unaffected individuals, then the mutation is likely to be the causative agent of the particular disease. Comparison of affected and unaffected individuals generally involves first looking for structural alterations in the chromosomes such as deletions or translocations that are visible from chromosome spreads or detectable using PCR based on that DNA sequence. Ultimately, complete sequencing of genes from several individuals can be performed to confirm the presence of a mutation and to distinguish mutations from polymorphisms.

## 2. Tissue Typing

The Tango-77 sequences of the present invention can also be used to identify individuals from minute biological samples. The United States military, for example, is considering the use of restriction fragment length polymorphism (RFLP) for identification of its personnel. In this technique, an individual's genomic DNA is digested with one or more restriction enzymes, and probed on a Southern blot to yield unique bands for identification. This method does not suffer from the current limitations of "Dog Tags" which can be lost, switched, or stolen, making positive identification difficult. The sequences of the present invention are useful as additional DNA markers for RFLP (described in U.S. Patent 5,272,057).

Furthermore, the sequences of the present invention can be used to provide an alternative technique which determines the actual base-by-base DNA sequence of selected portions of an individual's genome. Thus, the Tango-77 sequences described herein can be used to prepare two PCR primers from the 5' and 3' ends of the

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sequences. These primers can then be used to amplify an individual's DNA and subsequently sequence it.

Panels of corresponding DNA sequences from individuals, prepared in this manner, can provide unique individual identifications, as each individual will have a unique set of such DNA sequences due to allelic differences. The sequences of the present invention can be used to obtain such identification sequences from individuals and from tissue. The Tango-77 sequences of the invention uniquely represent portions of the human genome. Allelic variation occurs to some degree in the coding regions of these sequences, and to a greater degree in the noncoding regions. It is estimated that allelic variation between individual humans occurs with a frequency of about once per each 500 bases. Each of the sequences described herein can, to some degree, be used as a standard against which DNA from an individual can be compared for identification purposes. Because greater numbers of polymorphisms occur in the noncoding regions, fewer sequences are necessary to differentiate individuals. The noncoding sequences of SEQ ID NO:1 can comfortably provide positive individual identification with a panel of perhaps 10 to 1,000 primers which each yield a noncoding amplified sequence of 100 bases. If predicted coding sequences, such as those in SEQ ID NO:3, SEQ ID NO:6, or SEQ ID NO:10 are used, a more appropriate number of primers for positive individual identification would be 500-2,000.

If a panel of reagents from Tango-77 sequences described herein is used to generate a unique identification database for an individual, those same reagents can later be used to identify tissue from that individual. Using the unique identification database, positive identification of the individual, living or dead, can be made from extremely small tissue samples.

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### 3. Use of Partial Tango-77 Sequences in Forensic Biology

DNA-based identification techniques can also be used in forensic biology. Forensic biology is a scientific field employing genetic typing of biological evidence found at a crime scene as a means for positively identifying, for example, a perpetrator of a crime. To make such an identification, PCR technology can be used to amplify DNA sequences taken from very small biological samples such as tissues, e.g., hair or skin, or body fluids, e.g., blood, saliva, or semen found at a crime scene. The amplified sequence can then be compared to a standard, thereby allowing identification of the origin of the biological sample.

The sequences of the present invention can be used to provide polynucleotide reagents, e.g., PCR primers, targeted to specific loci in the human genome, which can enhance the reliability of DNA-based forensic identifications by, for example, providing another "identification marker" (i.e. another DNA sequence that is unique to a particular individual). As mentioned above, actual base sequence information can be used for identification as an accurate alternative to patterns formed by restriction enzyme generated fragments. Sequences targeted to noncoding regions of SEQ ID NO:1 are particularly appropriate for this use as greater numbers of polymorphisms occur in the noncoding regions, making it easier to differentiate individuals using this technique. Examples of polynucleotide reagents include the Tango-77 sequences or portions thereof, e.g., fragments derived from the noncoding regions of SEQ ID NO:1 having a length of at least 20 or 30 bases.

The Tango-77 sequences described herein can further be used to provide polynucleotide reagents, e.g., labeled or labelable probes which can be used in, for

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example, an in situ hybridization technique, to identify a specific tissue, e.g., brain tissue. This can be very useful in cases where a forensic pathologist is presented with a tissue of unknown origin. Panels of such Tango-77 probes can be used to identify tissue by species and/or by organ type.

In a similar fashion, these reagents, e.g., Tango-77 primers or probes can be used to screen tissue culture for contamination (i.e., screen for the presence of a mixture of different types of cells in a culture).

### C. Predictive Medicine

The present invention also pertains to the field of predictive medicine in which diagnostic assays, prognostic assays, pharmacogenomics, and monitoring clinical trials are used for prognostic (predictive) purposes to thereby treat an individual prophylactically. Accordingly, one aspect of the present invention relates to diagnostic assays for determining Tango-77 protein and/or nucleic acid expression as well as Tango-77 activity, in the context of a biological sample (e.g., blood, serum, cells, tissue) to thereby determine whether an individual is afflicted with a disease or disorder, or is at risk of developing a disorder, associated with aberrant Tango-77 expression or activity. The invention also provides for prognostic (or predictive) assays for determining whether an individual is at risk of developing a disorder associated with Tango-77 protein, nucleic acid expression or activity. For example, mutations in a Tango-77 gene can be assayed in a biological sample. Such assays can be used for prognostic or predictive purpose to thereby prophylactically treat an individual prior to the onset of a disorder characterized by or associated with Tango-77 protein, nucleic acid expression or activity.



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Another aspect of the invention provides methods for determining Tango-77 protein, nucleic acid expression or Tango-77 activity in an individual to thereby select appropriate therapeutic or prophylactic agents for that individual (referred to herein as "pharmacogenomics"). Pharmacogenomics allows for the selection of agents (e.g., drugs) for therapeutic or prophylactic treatment of an individual based on the genotype of the individual (e.g., the genotype of the individual examined to determine the ability of the individual to respond to a particular agent.)

Yet another aspect of the invention pertains to monitoring the influence of agents (e.g., drugs or other compounds) on the expression or activity of Tango-77 in clinical trials.

These and other agents are described in further detail in the following sections.

#### 1. Diagnostic Assays

An exemplary method for detecting the presence or absence of Tango-77 in a biological sample involves obtaining a biological sample from a test subject and contacting the biological sample with a compound or an agent capable of detecting Tango-77 protein or nucleic acid (e.g., mRNA, genomic DNA) that encodes Tango-77 protein such that the presence of Tango-77 is detected in the biological sample. A preferred agent for detecting Tango-77 mRNA or genomic DNA is a labeled nucleic acid probe capable of hybridizing to Tango-77 mRNA or genomic DNA. The nucleic acid probe can be, for example, a full-length Tango-77 nucleic acid, such as the nucleic acid of SEQ ID NO: 1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10 or a portion thereof, such as an oligonucleotide of at least 15, 30, 50, 100, 250 or 500 nucleotides in length and sufficient to specifically hybridize under stringent

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conditions to Tango-77 mRNA or genomic DNA. Other suitable probes for use in the diagnostic assays of the invention are described herein.

A preferred agent for detecting Tango-77 protein is an antibody capable of binding to Tango-77 protein, preferably an antibody with a detectable label. Antibodies can be polyclonal, or more preferably, monoclonal. An intact antibody, or a fragment thereof (e.g., Fab or F(ab')<sub>2</sub>) can be used. The term "labeled", with regard to the probe or antibody, is intended to encompass direct labeling of the probe or antibody by coupling (i.e., physically linking) a detectable substance to the probe or antibody, as well as indirect labeling of the probe or antibody by reactivity with another reagent that is directly labeled. Examples of indirect labeling include detection of a primary antibody using a fluorescently labeled secondary antibody and end-labeling of a DNA probe with biotin such that it can be detected with fluorescently labeled streptavidin. The term "biological sample" is intended to include tissues, cells and biological fluids isolated from a subject, as well as tissues, cells and fluids present within a subject. That is, the detection method of the invention can be used to detect Tango-77 mRNA, protein, or genomic DNA in a biological sample in vitro as well as in vivo. For example, in vitro techniques for detection of Tango-77 mRNA include Northern hybridizations and in situ hybridizations. In vitro techniques for detection of Tango-77 protein include enzyme linked immunosorbent assays (ELISAs), Western blots, immunoprecipitations and immunofluorescence. In vitro techniques for detection of Tango-77 genomic DNA include Southern hybridizations. Furthermore, in vivo techniques for detection of Tango-77 protein include introducing into a subject a labeled anti-Tango-77 antibody. For example, the antibody can be

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labeled with a radioactive marker whose presence and location in a subject can be detected by standard imaging techniques..

In one embodiment, the biological sample contains  
5 protein molecules from the test subject. Alternatively, the biological sample can contain mRNA molecules from the test subject or genomic DNA molecules from the test subject. A preferred biological sample is a peripheral blood leukocyte sample isolated by conventional means  
10 from a subject.

In another embodiment, the methods further involve obtaining a control biological sample from a control subject, contacting the control sample with a compound or agent capable of detecting Tango-77 protein, mRNA, or  
15 genomic DNA, such that the presence of Tango-77 protein, mRNA or genomic DNA is detected in the biological sample, and comparing the presence of Tango-77 protein, mRNA or genomic DNA in the control sample with the presence of Tango-77 protein, mRNA or genomic DNA in the test sample.

20 The invention also encompasses kits for detecting the presence of Tango-77 in a biological sample (a test sample). Such kits can be used to determine if a subject is suffering from or is at increased risk of developing a disorder associated with aberrant expression of Tango-77  
25 (e.g., an immunological disorder). For example, the kit can comprise a labeled compound or agent capable of detecting Tango-77 protein or mRNA in a biological sample and means for determining the amount of Tango-77 in the sample (e.g., an anti-Tango-77 antibody or an  
30 oligonucleotide probe which binds to DNA encoding Tango-77, e.g., SEQ ID NO:1 or SEQ ID NO:3 or SEQ ID NO:6, or SEQ ID NO:10). Kits may also include instruction for observing that the tested subject is suffering from or is at risk of developing a disorder  
35 associated with aberrant expression of Tango-77 if the

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amount of Tango-77 protein or mRNA is above or below a normal level.

For antibody-based kits, the kit may comprise, for example: (1) a first antibody (e.g., attached to a solid support) which binds to Tango-77 protein; and, optionally (2) a second, different antibody which binds to Tango-77 protein or the first antibody and is conjugated to a detectable agent.

For oligonucleotide-based kits, the kit may comprise, for example: (1) an oligonucleotide, e.g., a detectably labelled oligonucleotide, which hybridizes to a Tango-77 nucleic acid sequence or (2) a pair of primers useful for amplifying a Tango-77 nucleic acid molecule;

The kit may also comprise, e.g., a buffering agent, a preservative, or a protein stabilizing agent. The kit may also comprise components necessary for detecting the detectable agent (e.g., an enzyme or a substrate). The kit may also contain a control sample or a series of control samples which can be assayed and compared to the test sample contained. Each component of the kit is usually enclosed within an individual container and all of the various containers are within a single package along with instructions for observing whether the tested subject is suffering from or is at risk of developing a disorder associated with aberrant expression of Tango-77.

## 2. Prognostic Assays

The methods described herein can furthermore be utilized as diagnostic or prognostic assays to identify subjects having or at risk of developing a disease or disorder associated with aberrant Tango-77 expression or activity. For example, the assays described herein, such as the preceding diagnostic assays or the following assays, can be utilized to identify a subject having or

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at risk of developing a disorder associated with aberrant expression or activity. Thus, the present invention provides a method in which a test sample is obtained from a subject and Tango-77 protein or nucleic acid (e.g.,  
5 mRNA, genomic DNA) is detected, wherein the presence of Tango-77 protein or nucleic acid is diagnostic for a subject having or at risk of developing a disease or disorder associated with aberrant Tango-77 expression or activity. As used herein, a "test sample" refers to a  
10 biological sample obtained from a subject of interest. For example, a test sample can be a biological fluid (e.g., serum), cell sample, or tissue.

Furthermore, the prognostic assays described herein can be used to determine whether a subject can be  
15 administered an agent (e.g., an agonist, antagonist, peptidomimetic, protein, peptide, nucleic acid, small molecule, or other drug candidate) to treat a disease or disorder associated with aberrant Tango-77 expression or activity. For example, such methods can be used to  
20 determine whether a subject can be effectively treated with a specific agent or class of agents (e.g., agents of a type which decrease Tango-77 activity). Thus, the present invention provides methods for determining whether a subject can be effectively treated with an  
25 agent for a disorder associated with aberrant Tango-77 expression or activity in which a test sample is obtained and Tango-77 protein or nucleic acid is detected (e.g., wherein the presence of Tango-77 protein or nucleic acid is diagnostic for a subject that can be administered the  
30 agent to treat a disorder associated with aberrant Tango-77 expression or activity).

The methods of the invention can also be used to detect genetic lesions or mutations in a Tango-77 gene, thereby determining if a subject with the lesioned gene  
35 is at risk for a disorder characterized by aberrant

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inflammation. In preferred embodiments, the methods include detecting, in a sample of cells from the subject, the presence or absence of a genetic lesion or mutation characterized by at least one of an alteration affecting  
5 the integrity of a gene encoding a Tango-77-protein, or the mis-expression of the Tango-77 gene. For example, such genetic lesions or mutations can be detected by ascertaining the existence of at least one of: 1) a deletion of one or more nucleotides from a Tango-77 gene;  
10 2) an addition of one or more nucleotides to a Tango-77 gene; 3) a substitution of one or more nucleotides of a Tango-77 gene; 4) a chromosomal rearrangement of a Tango-77 gene; 5) an alteration in the level of a messenger RNA transcript of a Tango-77 gene; 6) an  
15 aberrant modification of a Tango-77 gene, such as of the methylation pattern of the genomic DNA; 7) the presence of a non-wild type splicing pattern of a messenger RNA transcript of a Tango-77 gene; 8) a non-wild type level of a Tango-77-protein; 9) an allelic loss of a Tango-77  
20 gene, and 10) an inappropriate post-translational modification of a Tango-77-protein. As described herein, there are a large number of assay techniques known in the art which can be used for detecting lesions or mutations in a Tango-77 gene. A preferred biological sample is a  
25 peripheral blood leukocyte sample isolated by conventional means from a subject.

In certain embodiments, detection of the lesion involves the use of a probe/primer in a polymerase chain reaction (PCR) (see, e.g., U.S. Patent Nos. 4,683,195 and  
30 4,683,202), such as anchor PCR or RACE PCR, or, alternatively, in a ligation chain reaction (LCR) (see, e.g., Landegran et al. (1988) *Science* 241:1077-1080; and Nakazawa et al. (1994) *Proc. Natl. Acad. Sci. USA* 91:360-364), the latter of which can be particularly useful for  
35 detecting point mutations in the Tango-77-gene (see,

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e.g., Abravaya et al. (1995) *Nucleic Acids Res.* 23:675-682). This method can include the steps of collecting a sample of cells from a patient, isolating nucleic acid (e.g., genomic, mRNA or both) from the cells of the  
5 sample, contacting the nucleic acid sample with one or more primers which specifically hybridize to a Tango-77 gene under conditions such that hybridization and amplification of the Tango-77-gene (if present) occurs, and detecting the presence or absence of an amplification  
10 product, or detecting the size of the amplification product and comparing the length to a control sample. It is anticipated that PCR and/or LCR may be desirable to use as a preliminary amplification step in conjunction with any of the techniques used for detecting mutations  
15 described herein.

Alternative amplification methods include: self sustained sequence replication (Guatelli et al. (1990) *Proc. Natl. Acad. Sci. USA* 87:1874-1878), transcriptional amplification system (Kwoh, et al. (1989) *Proc. Natl.*  
20 *Acad. Sci. USA* 86:1173-1177), Q-Beta Replicase (Lizardi et al. (1988) *Bio/Technology* 6:1197), or any other nucleic acid amplification method, followed by the detection of the amplified molecules using techniques well known to those of skill in the art. These detection  
25 schemes are especially useful for the detection of nucleic acid molecules if such molecules are present in very low numbers.

In an alternative embodiment, mutations in a Tango-77 gene from a sample cell can be identified by  
30 alterations in restriction enzyme cleavage patterns. For example, sample and control DNA is isolated, amplified (optionally), digested with one or more restriction endonucleases, and fragment length sizes are determined by gel electrophoresis and compared. Differences in  
35 fragment length sizes between sample and control DNA

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indicates mutations in the sample DNA. Moreover, the use of sequence specific ribozymes (see, e.g., U.S. Patent No. 5,498,531) can be used to score for the presence of specific mutations by development or loss of a ribozyme cleavage site.

In other embodiments, genetic mutations in Tango-77 can be identified by hybridizing a sample and control nucleic acids, e.g., DNA or RNA, to high density arrays containing hundreds or thousands of oligonucleotides probes (Cronin et al. (1996) *Human Mutation* 7:244-255; Kozal et al. (1996) *Nature Medicine* 2:753-759). For example, genetic mutations in Tango-77 can be identified in two-dimensional arrays containing light-generated DNA probes as described in Cronin et al. supra. Briefly, a first hybridization array of probes can be used to scan through long stretches of DNA in a sample and control to identify base changes between the sequences by making linear arrays of sequential overlapping probes. This step allows the identification of point mutations. This step is followed by a second hybridization array that allows the characterization of specific mutations by using smaller, specialized probe arrays complementary to all variants or mutations detected. Each mutation array is composed of parallel probe sets, one complementary to the wild-type gene and the other complementary to the mutant gene.

In yet another embodiment, any of a variety of sequencing reactions known in the art can be used to directly sequence the Tango-77 gene and detect mutations by comparing the sequence of the sample Tango-77 with the corresponding wild-type (control) sequence. Examples of sequencing reactions include those based on techniques developed by Maxim and Gilbert ((1977) *Proc. Natl. Acad. Sci. USA* 74:560) or Sanger ((1977) *Proc. Natl. Acad. Sci. USA* 74:5463). It is also contemplated that any of a



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variety of automated sequencing procedures can be utilized when performing the diagnostic assays ((1995) *Bio/Techniques* 19:448), including sequencing by mass spectrometry (see, e.g., PCT Publication No. WO 94/16101; 5 Cohen et al. (1996) *Adv. Chromatogr.* 36:127-162; and Griffin et al. (1993) *Appl. Biochem. Biotechnol.* 38:147-159).

Other methods for detecting mutations in the Tango-77 gene include methods in which protection from 10 cleavage agents is used to detect mismatched bases in RNA/RNA or RNA/DNA heteroduplexes (Myers et al. (1985) *Science* 230:1242). In general, the technique of "mismatch cleavage" entails providing heteroduplexes formed by hybridizing (labeled) RNA or DNA containing the 15 wild-type Tango-77 sequence with potentially mutant RNA or DNA obtained from a tissue sample. The double-stranded duplexes are treated with an agent which cleaves single-stranded regions of the duplex such as which will exist due to basepair mismatches between the control and 20 sample strands. RNA/DNA duplexes can be treated with RNase to digest mismatched regions, and DNA/DNA hybrids can be treated with S1 nuclease to digest mismatched regions. In other embodiments, either DNA/DNA or RNA/DNA duplexes can be treated with hydroxylamine or osmium 25 tetroxide and with piperidine in order to digest mismatched regions. After digestion of the mismatched regions, the resulting material is then separated by size on denaturing polyacrylamide gels to determine the site of mutation. See, e.g., Cotton et al. (1988) *Proc. Natl. Acad. Sci. USA* 85:4397; Saleeba et al. (1992) *Methods Enzymol.* 217:286-295. In a preferred embodiment, the 30 control DNA or RNA can be labeled for detection.

In still another embodiment, the mismatch cleavage reaction employs one or more proteins that recognize 35 mismatched base pairs in double-stranded DNA (so called

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"DNA mismatch repair" enzymes) in defined systems for detecting and mapping point mutations in Tango-77 cDNAs obtained from samples of cells. For example, the mutY enzyme of *E. coli* cleaves A at G/A mismatches and the  
5 thymidine DNA glycosylase from HeLa cells cleaves T at G/T mismatches (Hsu et al. (1994) *Carcinogenesis* 15:1657-1662). According to an exemplary embodiment, a probe based on a Tango-77 sequence, e.g., a wild-type Tango-77 sequence, is hybridized to a cDNA or other DNA product  
10 from a test cell(s). The duplex is treated with a DNA mismatch repair enzyme, and the cleavage products, if any, can be detected from electrophoresis protocols or the like. See, e.g., U.S. Patent No. 5,459,039.

In other embodiments, alterations in  
15 electrophoretic mobility will be used to identify mutations in Tango-77 genes. For example, single strand conformation polymorphism (SSCP) may be used to detect differences in electrophoretic mobility between mutant and wild type nucleic acids (Orita et al. (1989) *Proc.*  
20 *Natl. Acad. Sci. USA* 86:2766; see also Cotton (1993) *Mutat. Res.* 285:125-144; Hayashi (1992) *Genet Anal Tech Appl* 9:73-79). Single-stranded DNA fragments of sample and control Tango-77 nucleic acids will be denatured and allowed to renature. The secondary structure of single-  
25 stranded nucleic acids varies according to sequence, and the resulting alteration in electrophoretic mobility enables the detection of even a single base change. The DNA fragments may be labeled or detected with labeled probes. The sensitivity of the assay may be enhanced by  
30 using RNA (rather than DNA), in which the secondary structure is more sensitive to a change in sequence. In a preferred embodiment, the subject method utilizes heteroduplex analysis to separate double stranded heteroduplex molecules on the basis of changes in

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electrophoretic mobility (Keen et al. (1991) *Trends Genet* 7:5).

In yet another embodiment, the movement of mutant or wild-type fragments in polyacrylamide gels containing a gradient of denaturant is assayed using denaturing gradient gel electrophoresis (DGGE) (Myers et al. (1985) *Nature* 313:495). When DGGE is used as the method of analysis, DNA will be modified to insure that it does not completely denature, for example by adding a GC clamp of approximately 40 bp of high-melting GC-rich DNA by PCR. In a further embodiment, a temperature gradient is used in place of a denaturing gradient to identify differences in the mobility of control and sample DNA (Rosenbaum and Reissner (1987) *Biophys. Chem.* 265:12753).

Examples of other techniques for detecting point mutations include, but are not limited to, selective oligonucleotide hybridization, selective amplification, or selective primer extension. For example, oligonucleotide primers may be prepared in which the known mutation is placed centrally and then hybridized to target DNA under conditions which permit hybridization only if a perfect match is found (Saiki et al. (1986) *Nature* 324:163); Saiki et al. (1989) *Proc. Natl. Acad. Sci. USA* 86:6230). Such allele specific oligonucleotides are hybridized to PCR amplified target DNA or a number of different mutations when the oligonucleotides are attached to the hybridizing membrane and hybridized with labeled target DNA.

Alternatively, allele specific amplification technology which depends on selective PCR amplification may be used in conjunction with the instant invention. Oligonucleotides used as primers for specific amplification may carry the mutation of interest in the center of the molecule (so that amplification depends on differential hybridization) (Gibbs et al. (1989) *Nucleic*

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*Acids Res.* 17:2437-2448) or at the extreme 3' end of one primer where, under appropriate conditions, mismatch can prevent or reduce polymerase extension (Prossner (1993) *Tibtech* 11:238). In addition, it may be desirable to  
5 introduce a novel restriction site in the region of the mutation to create cleavage-based detection (Gasparini et al. (1992) *Mol. Cell Probes* 6:1). It is anticipated that in certain embodiments amplification may also be performed using Taq ligase for amplification (Barany  
10 (1991) *Proc. Natl. Acad. Sci USA* 88:189). In such cases, ligation will occur only if there is a perfect match at the 3' end of the 5' sequence making it possible to detect the presence of a known mutation at a specific site by looking for the presence or absence of  
15 amplification.

The methods described herein may be performed, for example, by utilizing pre-packaged diagnostic kits comprising at least one probe nucleic acid or antibody reagent described herein, which may be conveniently used,  
20 e.g., in clinical settings to diagnose patients exhibiting symptoms or family history of a disease or illness involving a Tango-77 gene.

Furthermore, any cell type or tissue, preferably peripheral blood leukocytes, in which Tango-77 is  
25 expressed may be utilized in the prognostic assays described herein.

### 3. Pharmacogenomics

Agents, or modulators which have a stimulatory or  
30 inhibitory effect on Tango-77 activity (e.g., Tango-77 gene expression) as identified by a screening assay described herein can be administered to individuals to treat (prophylactically or therapeutically) disorders (e.g., acute or chronic inflammation and asthma)  
35 associated with aberrant Tango-77 activity. In

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conjunction with such treatment, the pharmacogenomics (i.e., the study of the relationship between an individual's genotype and that individual's response to a foreign compound or drug) of the individual may be considered. Differences in metabolism of therapeutics can lead to severe toxicity or therapeutic failure by altering the relation between dose and blood concentration of the pharmacologically active drug. Thus, the pharmacogenomics of the individual permits the selection of effective agents (e.g., drugs) for prophylactic or therapeutic treatments based on a consideration of the individual's genotype. Such pharmacogenomics can further be used to determine appropriate dosages and therapeutic regimens. Accordingly, the activity of Tango-77 protein, expression of Tango-77 nucleic acid, or mutation content of Tango-77 genes in an individual can be determined to thereby select appropriate agent(s) for therapeutic or prophylactic treatment of the individual.

Pharmacogenomics deals with clinically significant hereditary variations in the response to drugs due to altered drug disposition and abnormal action in affected persons. See, e.g., Linder (1997) *Clin. Chem.* 43(2):254-266. In general, two types of pharmacogenetic conditions can be differentiated. Genetic conditions transmitted as a single factor altering the way drugs act on the body are referred to as "altered drug action." Genetic conditions transmitted as single factors altering the way the body acts on drugs are referred to as "altered drug metabolism". These pharmacogenetic conditions can occur either as rare defects or as polymorphisms. For example, glucose-6-phosphate dehydrogenase deficiency (G6PD) is a common inherited enzymopathy in which the main clinical complication is haemolysis after ingestion of oxidant drugs (anti-

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malarials, sulfonamides, analgesics, nitrofurans) and consumption of fava beans.

As an illustrative embodiment, the activity of drug metabolizing enzymes is a major determinant of both the intensity and duration of drug action. The discovery of genetic polymorphisms of drug metabolizing enzymes (e.g., N-acetyltransferase 2 (NAT 2) and cytochrome P450 enzymes CYP2D6 and CYP2C19) has provided an explanation as to why some patients do not obtain the expected drug effects or show exaggerated drug response and serious toxicity after taking the standard and safe dose of a drug. These polymorphisms are expressed in two phenotypes in the population, the extensive metabolizer (EM) and poor metabolizer (PM). The prevalence of PM is different among different populations. For example, the gene coding for CYP2D6 is highly polymorphic and several mutations have been identified in PM, which all lead to the absence of functional CYP2D6. Poor metabolizers of CYP2D6 and CYP2C19 quite frequently experience exaggerated drug response and side effects when they receive standard doses. If a metabolite is the active therapeutic moiety, PM shows no therapeutic response, as demonstrated for the analgesic effect of codeine mediated by its CYP2D6-formed metabolite morphine. The other extreme are the so called ultra-rapid metabolizers who do not respond to standard doses. Recently, the molecular basis of ultra-rapid metabolism has been identified to be due to CYP2D6 gene amplification.

Thus, the activity of Tango-77 protein, expression of Tango-77 nucleic acid, or mutation content of Tango-77 genes in an individual can be determined to thereby select appropriate agent(s) for therapeutic or prophylactic treatment of the individual. In addition, pharmacogenetic studies can be used to apply genotyping of polymorphic alleles encoding drug-metabolizing enzymes

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to the identification of an individual's drug responsiveness phenotype. This knowledge, when applied to dosing or drug selection, can avoid adverse reactions or therapeutic failure and thus enhance therapeutic or prophylactic efficiency when treating a subject with a Tango-77 modulator, such as a modulator identified by one of the exemplary screening assays described herein.

#### 4. Monitoring of Effects During Clinical Trials

Monitoring the influence of agents (e.g., drugs, compounds) on the expression or activity of Tango-77 (e.g., the ability to modulate aberrant inflammation) can be applied not only in basic drug screening, but also in clinical trials. For example, the effectiveness of an agent, as determined by a screening assay as described herein, to increase Tango-77 gene expression, increase protein levels, or upregulate Tango-77 activity, can be monitored in clinical trials of subjects exhibiting decreased Tango-77 gene expression, decreased protein levels, or downregulated Tango-77 activity. Alternatively, the effectiveness of an agent, as determined by a screening assay, to decrease Tango-77 gene expression, decrease protein levels, or downregulate Tango-77 activity, can be monitored in clinical trials of subjects exhibiting increased Tango-77 gene expression, increased protein levels, or upregulated Tango-77 activity.

For example, and not by way of limitation, genes, including Tango-77, that are modulated in cells by treatment with an agent (e.g., compound, drug or small molecule) which modulates Tango-77 activity (e.g., as identified in a screening assay described herein) can be identified. Thus, to study the effect of agents on cellular proliferation disorders, for example, in a clinical trial, cells can be isolated and RNA prepared

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and analyzed for the levels of expression of Tango-77 and other genes implicated in the disorder. The levels of gene expression (i.e., a gene expression pattern) can be quantified by Northern blot analysis or RT-PCR, as  
5 described herein, or alternatively by measuring the amount of protein produced, by one of the methods as described herein, or by measuring the levels of activity of Tango-77 or other genes. In this way, the gene expression pattern can serve as a marker, indicative of  
10 the physiological response of the cells to the agent. Accordingly, this response state may be determined before, and at various points during, treatment of the individual with the agent.

In a preferred embodiment, the present invention  
15 provides a method for monitoring the effectiveness of treatment of a subject with an agent (e.g., an agonist, antagonist, peptidomimetic, protein, peptide, nucleic acid, small molecule, or other drug candidate identified by the screening assays described herein) comprising the  
20 steps of (i) obtaining a pre-administration sample from a subject prior to administration of the agent; (ii) detecting the level of expression of a Tango-77 protein, mRNA, or genomic DNA in the preadministration sample; (iii) obtaining one or more post-administration samples  
25 from the subject; (iv) detecting the level of expression or activity of the Tango-77 protein, mRNA, or genomic DNA in the post-administration samples; (v) comparing the level of expression or activity of the Tango-77 protein, mRNA, or genomic DNA in the pre-administration sample  
30 with the Tango-77 protein, mRNA, or genomic DNA in the post administration sample or samples; and (vi) altering the administration of the agent to the subject accordingly. For example, increased administration of the agent may be desirable to increase the expression or  
35 activity of Tango-77 to higher levels than detected,



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i.e., to increase the effectiveness of the agent.  
Alternatively, decreased administration of the agent may  
be desirable to decrease expression or activity of  
Tango-77 to lower levels than detected, i.e., to decrease  
5 the effectiveness of the agent.

### C. Methods of Treatment

The present invention provides for both  
prophylactic and therapeutic methods of treating a  
subject at risk of (or susceptible to) developing or  
10 having a disorder associated with aberrant Tango-77  
expression or activity. Alternatively, disorders  
associated with aberrant IL-1 production can be treated  
with Tango-77. Such disorders include acute and chronic  
inflammation, asthma, some classes of arthritis,  
15 autoimmune diabetes, systemic lupus erythematosus and  
inflammatory bowel disease.

#### 1. Prophylactic Methods

In one aspect, the invention provides a method for  
preventing in a subject, a disease or condition  
20 associated with an aberrant Tango-77 expression or  
activity (or aberrant IL-1 expression or activity), by  
administering to the subject an agent which modulates  
Tango-77 expression or at least one Tango-77 activity.  
Subjects at risk for a disease which is caused or  
25 contributed to by aberrant Tango-77 expression or  
activity can be identified by, for example, any or a  
combination of diagnostic or prognostic assays as  
described herein. Administration of a prophylactic agent  
can occur prior to the manifestation of symptoms  
30 characteristic of the Tango-77 aberrancy, such that a  
disease or disorder is prevented or, alternatively,  
delayed in its progression. Depending on the type of  
Tango-77 aberrancy, for example, a Tango-77 agonist or  
Tango-77 antagonist agent can be used for treating the

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subject. The appropriate agent can be determined based on screening assays described herein.

## 2. Therapeutic Methods

Another aspect of the invention pertains to methods of modulating Tango-77 expression or activity for therapeutic purposes. The modulatory method of the invention involves contacting a cell with an agent that modulates one or more of the activities of Tango-77 protein activity associated with the cell. An agent that modulates Tango-77 protein activity can be an agent as described herein, such as a nucleic acid or a protein, a naturally-occurring cognate ligand of a Tango-77 protein, a peptide, a Tango-77 peptidomimetic, or other small molecule. In one embodiment, the agent stimulates one or more of the biological activities of Tango-77 protein. Examples of such stimulatory agents include active Tango-77 protein and a nucleic acid molecule encoding Tango-77 that has been introduced into the cell. In another embodiment, the agent inhibits one or more of the biological activities of Tango-77 protein. Examples of such inhibitory agents include antisense Tango-77 nucleic acid molecules and anti-Tango-77 antibodies. These modulatory methods can be performed in vitro (e.g., by culturing the cell with the agent) or, alternatively, in vivo (e.g., by administering the agent to a subject). As such, the present invention provides methods of treating an individual afflicted with a disease or disorder characterized by aberrant expression or activity of a Tango-77 protein or nucleic acid molecule. In one embodiment, the method involves administering an agent (e.g., an agent identified by a screening assay described herein), or combination of agents that modulates (e.g., upregulates or downregulates) Tango-77 expression or activity. In another embodiment, the method involves

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administering a Tango-77 protein or nucleic acid molecule as therapy to compensate for reduced or aberrant Tango-77 expression or activity.

Stimulation of Tango-77 activity is desirable in situations in which Tango-77 is abnormally downregulated and/or in which increased Tango-77 activity is likely to have a beneficial effect. Conversely, inhibition of Tango-77 activity is desirable in situations in which Tango-77 is abnormally upregulated and/or in which decreased Tango-77 activity is likely to have a beneficial effect.

This invention is further illustrated by the following examples which should not be construed as limiting. The contents of all references, patents and published patent applications cited throughout this application are hereby incorporated by reference.

#### EXAMPLES

##### Example 1: Isolation and Characterization of Human Tango-77 cDNAs

Cytokine genes IL-1 $\alpha$ , IL-1 $\beta$  and IL-1ra have been found to be closely clustered on chromosome 2, i.e., IL-1 $\alpha$ , IL-1 $\beta$  and IL-1ra are located within 450 kb of each other. BAC clones containing IL-1 $\alpha$  and IL-1 $\beta$  were used to identify other proximal unknown cytokine genes. To do this, a BAC clone containing IL-1 $\alpha$  and IL-1 $\beta$  was selected from a BAC library (Research Genetics, Huntsville, Alabama) using specific primers designed against IL-1 $\alpha$  and IL-1 $\beta$ . The DNA from the BAC was extracted and used to make a random-sheared genomic library. From this BAC library, 4000 clones were selected for sequencing. The resulting genomic sequences were then assembled into contigs and used to screen proprietary and public data bases. One genomic contig was found to contain two

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segments of sequences which resemble IL-1ra. These two segments are potential exons of Tango-77 gene.

Two PCR primers were then designed from the two potential exons and used to screen a panel of cDNA libraries for the expression of a Tango-77 message. A cDNA library from TNF- $\alpha$  treated human lung epithelia showed a positive band of the predicted size (i.e., if the two exons are spliced together). Using the PCR fragment as a probe, a single cDNA clone was isolated from the same library. This cDNA contains an insert of 989 bp. The cDNA clone contains three possible open reading frames. The first open reading frame encompasses 534 nucleotides (nucleotides 356-889 of SEQ ID NO:1; SEQ ID NO:3) and encodes a 178 amino acid protein (SEQ ID NO:2). This protein may include a predicted signal sequence of about 63 amino acids (from amino acid 1 to about amino acid 63 of SEQ ID NO:2 (SEQ ID NO:4)) and a predicted mature protein of about 115 amino acids (from about amino acid 64 to amino acid 178 of SEQ ID NO:2 (SEQ ID NO:5)).

The second putative nucleotide open reading frame encompasses 498 nucleotides (nucleotides 389-889 of SEQ ID NO:1; SEQ ID NO:6) and encodes a 167 amino acid protein (SEQ ID NO:7). This protein includes a predicted signal sequence of about 52 amino acids (from amino acid 1 to about amino acid 52 of SEQ ID NO:7 (SEQ ID NO:8)) and a predicted mature protein of about 115 amino acids (from about amino acid 53 to amino acid 167 of SEQ ID NO:7 (SEQ ID NO:9)).

The third open reading frame (nucleotides 372-889 of SEQ ID NO:1; SEQ ID NO:10) encompasses 408 nucleotides and encodes a 136 amino acid protein (SEQ ID NO:11). This protein includes a predicted signal sequence of about 21 amino acids (from amino acid 1 to about amino acid 21 of SEQ ID NO:11 (SEQ ID NO:12)) and a predicted

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mature protein of about 115 amino acids (from about amino acid 22 to amino acid 136 of SEQ ID NO:11 (SEQ ID NO:13)).

Tango-77 is predicted to be 35% identical to human IL-1ra at the amino acid level.

Example 2: Expression of Tango-77 mRNA in Human Tissues

The expression of Tango-77 was analyzed using Northern blot hybridization. A PCR generated 989 bp Tango-77 product was radioactively labeled with <sup>32</sup>P-dCTP using the Prime-It kit (Stratagene; La Jolla, CA) according to the instructions of the supplier. Filters containing human mRNA (MTNI and MTNII: Clontech; Palo Alto, CA) were probed in ExpressHyb hybridization solution (Clontech) and washed at high stringency according to manufacturer's recommendations.

Tango-77 mRNA was not detected in any unstimulated tissues (brain, liver, spleen, skeletal muscle, testis, pancreas, heart, kidney and peripheral blood leukocytes) mRNA on Clontech Northern blots.

Over 96 cDNA libraries were then tested for the presence of Tango-77 using PCR amplification. Only three libraries displayed a positive signal. These libraries were the TNF $\alpha$ -treated bronchoepithelium, TNF $\alpha$ -treated SSC cell line and anti-CD3-treated T cells.

Example 3: Characterization of Tango-77 Proteins

In this example, the predicted amino acid sequence of human Tango-77 protein was compared to the amino acid sequence of known protein IL-1ra. In addition, the molecular weight of the human Tango-77 proteins was predicted.

The human Tango-77 cDNA (Figure 1; SEQ ID NO:1) isolated as described above encodes a 178 amino acid protein (Figure 1; SEQ ID NO:2) or a 167 amino acid

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protein (Figure 1; SEQ ID NO:7) or a 136 amino acid protein (Figure 1; SEQ ID NO:11). The signal peptide prediction program SIGNALP Optimized Tool (Nielsen et al. (1997) *Protein Engineering* 10:1-6) predicted that

5 Tango-77 includes a 63 amino acid signal peptide (amino acid 1 to about amino acid 63 of SEQ ID NO:2 (SEQ ID NO:4)) preceding the 115 mature protein; or preceding the 115 mature protein (about amino acid 52 to amino acid 167 of SEQ ID NO:7 (SEQ ID NO:8)); or preceding the 115

10 mature protein (about amino acid 21 to amino acid 136 of SEQ ID NO:11;SEQ ID NO:12).

As shown in Figure 2, Tango-77 has a region of homology to IL-1ra (SEQ ID NO:14).

Mature Tango-77 has a predicted MW of about 13 kDa

15 and the predicted MW for the immature Tango-77 is 19.6 kDa, 18.5 kDa or 15.2 kDa, not including post-translational modifications.

#### Example 4: Preparation of Tango-77 Proteins

Recombinant Tango-77 can be produced in a variety

20 of expression systems. For example, the mature Tango-77 peptide can be expressed as a recombinant glutathione-S-transferase (GST) fusion protein in *E. coli* and the fusion protein can be isolated and characterized. Specifically, as described above, Tango-77 can be fused

25 to GST and this fusion protein can be expressed in *E. coli* strain PEB199. Expression of the GST-Tango-77 fusion protein in PEB199 can be induced with IPTG. The recombinant fusion protein can be purified from crude bacterial lysates of the induced PEB199 strain by

30 affinity chromatography on glutathione beads.

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Example 5: Alternatively spliced forms of IL-1ra and  
Tango-77

Computer program Procrustes (Gelfand et al., 1996, *Proc. Natl. Acad. Sci. USA*, 93:9061-9066) is an alignment  
5 algorithm that predicts the presence of alternatively  
spliced exons for a protein of interest in a stretch of  
genomic DNA. Using the IL-1ra sequence, Procrustes was  
used to search for the presence of additional sequences  
that might encode for alternatively spliced forms of IL-  
10 1ra in the two overlapping BAC genomic sequences (see  
Fig. 3 and Fig. 4). Potential sequences that encode  
variant exons for IL-1ra were identified. These  
predicted exons aligned well with the N-terminal region  
of IL-1ra, but were not present in Tango-77. The results  
15 from Procrustes predicts the existence of more spliced  
forms of IL-1ra.

Furthermore, Procrustes also predicted an  
additional sequence in BAC1 and BAC2 that encodes an  
alternatively spliced exon for Tango-77 (T77-procrustes;  
20 Fig. 5). This predicted splice variant form of Tango-77,  
T77-procrustes, was aligned with Tango-77 (Fig. 6) and  
with IL-1ra and IL-1 $\beta$  (Fig.7).

PCR primers within this sequence can be used to  
generate a product that can be used to screen a panel of  
25 cDNA libraries using standard techniques. Suitable cDNA  
libraries include libraries made from TNF $\alpha$ -treated  
bronchoepithelium, TNF $\alpha$ -treated SSC cell line and anti-  
CD3-treated T cells. The resulting cDNA clone(s) can be  
isolated from the library and sequenced to identify  
30 additional Tango-77 cDNAs.

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Equivalents

Those skilled in the art will recognize, or be able to ascertain using no more than routine experimentation, many equivalents to the specific s embodiments of the invention described herein. Such equivalents are intended to be encompassed by the following claims.



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What is claimed is:

1. An isolated nucleic acid molecule selected from the group consisting of:

- a) a nucleic acid molecule comprising a  
5 nucleotide sequence which is at least 45% identical to the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, the cDNA insert of the plasmid deposited with ATCC as Accession Number 98807, or a complement thereof;
- 10 b) a nucleic acid molecule comprising a fragment of at least 300 nucleotides of the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, the cDNA insert of the plasmid deposited with ATCC as Accession Number 98807, or a complement thereof;
- 15 c) nucleic acid molecule which encodes a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or an amino acid sequence encoded by the cDNA insert of the  
20 plasmid deposited with ATCC as Accession Number 98807;
- d) a nucleic acid molecule which encodes a fragment of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID  
25 NO:12, SEQ ID NO:13, wherein the fragment comprises at least 15 contiguous amino acids of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or the polypeptide encoded by the cDNA insert of the plasmid  
30 deposited with ATCC as Accession Number 98807; and
- e) a nucleic acid molecule which encodes a naturally occurring allelic variant of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9,

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SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or an amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Accession Number 98807, wherein the nucleic acid molecule hybridizes to a nucleic acid  
5 molecule comprising SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, or the complement thereof under stringent conditions.

2. The isolated nucleic acid molecule of claim 1, which is selected from the group consisting of:

10 a) a nucleic acid comprising the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, or SEQ ID NO:10 or the cDNA insert of the plasmid deposited with ATCC as Accession Number 98807, or a complement thereof; and

15 b) a nucleic acid molecule which encodes a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or an amino acid sequence encoded by the cDNA insert of the  
20 plasmid deposited with ATCC as Accession Number 98807.

3. The nucleic acid molecule of claim 1 further comprising vector nucleic acid sequences.

4. The nucleic acid molecule of claim 1 further comprising nucleic acid sequences encoding a heterologous  
25 polypeptide.

5. A host cell containing the nucleic acid molecule of claim 1.

6. The host cell of claim 5 which is a mammalian host cell.

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7. A non-human mammalian host cell containing the nucleic acid molecule of claim 1.

8. An isolated polypeptide selected from the group consisting of:

5 a) a fragment of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, wherein the fragment comprises at least 15 contiguous amino acids of SEQ ID  
10 NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, or SEQ ID NO:13.

b) a naturally occurring allelic variant of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8,  
15 SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or an amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Accession Number 98807, wherein the polypeptide is encoded by a nucleic acid molecule which hybridizes to a nucleic acid molecule  
20 comprising SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10 or the complement thereof under stringent conditions;

c) a polypeptide which is encoded by a nucleic acid molecule comprising a nucleotide sequence which is  
25 at least 55% identical to a nucleic acid comprising the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, or SEQ ID NO:10.

9. The isolated polypeptide of claim 8 comprising the amino acid sequence of SEQ ID NO:2, SEQ ID  
30 NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or an amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Accession Number 98807.

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10. The polypeptide of claim 8 further comprising heterologous amino acid sequences.

11. An antibody which selectively binds to a polypeptide of claim 8.

5 12. A method for producing a polypeptide selected from the group consisting of:

a) a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID  
10 NO:12, SEQ ID NO:13, or an amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Accession Number 98807;

b) a fragment of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID  
15 NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or an amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Accession Number 98807, wherein the fragment comprises at least 15 contiguous amino acids  
20 of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or an amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Accession Number 98807; and

25 c) a naturally occurring allelic variant of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or an amino acid sequence encoded by the cDNA insert of the  
30 plasmid deposited with ATCC as Accession Number 98807, wherein the polypeptide is encoded by a nucleic acid molecule which hybridizes to a nucleic acid sequence of

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SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, or SEQ ID NO:10  
under stringent conditions;

comprising culturing the host cell of claim 5  
under conditions in which the nucleic acid molecule is  
5 expressed.

13. A method for detecting the presence of a  
polypeptide of claim 8 in a sample, comprising:

- a) contacting the sample with a compound which  
selectively binds to a polypeptide of claim 8; and
- 10 b) determining whether the compound binds to the  
polypeptide in the sample.

14. The method of claim 13, wherein the compound  
which binds to the polypeptide is an antibody.

15 15. A kit comprising a compound which selectively  
binds to a polypeptide of claim 8 and instructions for  
use.

16. A method for detecting the presence of a  
nucleic acid molecule of claim 1 in a sample, comprising  
the steps of:

- 20 a) contacting the sample with a nucleic acid  
probe or primer which selectively hybridizes to the  
nucleic acid molecule; and
- b) determining whether the nucleic acid probe or  
primer binds to a nucleic acid molecule in the sample.

25 17. The method of claim 16, wherein the sample  
comprises mRNA molecules and is contacted with a nucleic  
acid probe.

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18. A kit comprising a compound which selectively hybridizes to a nucleic acid molecule of claim 1 and instructions for use.

19. A method for identifying a compound which  
s binds to a polypeptide of claim 8 comprising the steps of:

- a) contacting a polypeptide, or a cell expressing a polypeptide of claim 8 with a test compound; and
- 10 b) determining whether the polypeptide binds to the test compound.

20. The method of claim 19, wherein the binding of the test compound to the polypeptide is detected by a method selected from the group consisting of:

- 15 a) detection of binding by direct detecting of test compound/polypeptide binding;
- b) detection of binding using a competition binding assay; and
- c) detection of binding using an assay for  
20 Tango-77-mediated signal transduction.s

21. A method for modulating the activity of a polypeptide of claim 8 comprising contacting a polypeptide or a cell expressing a polypeptide of claim 8 with a compound which binds to the polypeptide in a  
25 sufficient concentration to modulate the activity of the polypeptide.

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22. A method for identifying a compound which modulates the activity of a polypeptide of claim 8, comprising:

- a) contacting a polypeptide of claim 8 with a  
5 test compound; and
- b) determining the effect of the test compound on the activity of the polypeptide to thereby identify a compound which modulates the activity of the polypeptide.

```

GTGACCCACGCGTCCGCAGACGTCTACCTGGGGGTCCCGTCTGCGCTCCCGGGATGGAAAACGCCCAGGGGAACTTA 79
GGCAGGCGAGCGGACGGGCACCTCCCGCGGGACGAACTCACTCGGTGGCCTCCTACTTCCCGGGCCGTGTTCCAACGCC 158
TGAGAATAACGGGAACAGCGGTCTACTCACCACAGCGGCAGCAGCGGCCTCTCTCAATTGGGCAAAGCACTCCAGAC 237
A TTTTGGGAAGAGTGACACCAAAGCAAGCACCTGCTTGGCAGGCCCTCAGCTTCTACGCAAGTATAAGTCTTGGACTT 316
CATTCGATTTTCTGTTGAGTAATAAACTCAACGTTGAAA M S F V G E N S G V 10
ATG TCC TTT GTG GGG GAG AAC TCA GGA GTG 385
K M E S E D W E K D E P Q C C L E D P A 30
AAA ATG GGC TCT GAG GAC TGG GAA AAA GAT GAA CCC CAG TGC TGC TTA GAA GAC CCG GCT 445
G S P L E P G P S L P T M N F V H T K I 50
GGA AGC CCC CTG GAA CCA GGC CCA AGC CTC CCC ACC ATG AAT TTT GTT CAC ACA AAG ATC 505
F F A L A S S L S S A S A E K G S P I L 70
TTC TTT GCA TTA GCC TCA TCC TTG AGC TCA GCC TCT GCG GAG AAA GGA AGT CCG ATT CTC 565
L G Y S K G E F C L Y C D K D K G Q S H 90
CTG GGG GTC TCT AAA GGG GAG TTT TGT CTC TAC TGT GAC AAG GAT AAA GGA CAA AGT CAT 625
P S L Q L K K E K L M K L A A Q K E S A 110
CCA TCC CTT CAG CTG AAG AAG GAG AAA CTG ATG AAG CTG GCT GCC CAA AAG GAA TCA GCA 685
R E P F I F Y R A Q Y G S W N M L E S A 130
CGC CCG CCC TTC ATC TTT TAT AGG GCT CAG GTG GGC TCC TGG AAC ATG CTG GAG TCG GCG 745
A H P G W F I C T S C N C N E P V G V T 150
GCT CAC CCC GGA TGG TTC ATC TGC ACC TCC TGC AAT TGT AAT GAG CCT GTT GGG GTG ACA 805
D K F E N R K H I E F S F Q P V C K A E 170
GAT AAA TTT GAG AAC AGG AAA CAC ATT GAA TTT TCA TTT CAA CCA GTT TGC AAA GCT GAA 865
M S P S E V S D * 179
ATG AGC CCC AGT GAG GTC AGC GAT TAG 892
GAAACTGCCCCATTGAACGCCCTTCCTCGCTAATTTGAACTAATTGTATAAAAAACACCAACCTGCTCACTAAAAA 971
AAAAAAAAGGGCGGCGGC 989

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Fig. 1



1 50  
 IL1ra-human MEICRGLRSH LITLLFLFH SETICRPSGR KSKMQAFRI WDVNQKTFYL  
 T77-human  
 IL1b-human  
 Consensus  
 51 100  
 IL1ra-human RNNQLVAGYL QGPNVNLEEK IDVVPFIEPH. ALFLGIHGGK MCLSCVKSGD  
 T77-human  
 IL1b-human  
 Consensus  
 101 150  
 IL1ra-human ETR..LQLEA VNITDLSNR KQDKR.FAFI RSDSGPTTSF ESAACPGWFL  
 T77-human QSHPSLQLKK EKLMKLAQK ESARRPFIFY RAQVGSWNML ESAAHPEWFI  
 IL1b-human K..PTLQLES VDPKNYP..K KMEKRPFVFN KIEINNKLFF ESAQFPNWI  
 Consensus  
 151 192  
 IL1ra-human CTAMEADQPV SLTNMPDEGV MVTKFYFQED E-----  
 T77-human CTSCNCNEPV GVTDKFENRK HI.EFSFPV CKAMPSEV SD  
 IL1b-human STSQAENMPV FLGGT.KGGQ DITDFTNQFV SS-----  
 Consensus -T-----PV -----F--Q--

FIG. 2

&gt;Contig1

GAAGTGAAGATATAATGTATAGTAGTAATATATAATGTTAGGTGAATTAA  
AGGAAATAGAATATATTGGGGAGTAATTATGGGTGTAAAGAAATATAGTA  
GGGAAGTATTAGATTTGAGAAAAAAGGAATTTAGTGTAGGTGAA  
NAATAAAAGNANAAGGTTAAAAATTAATAAATAAATAAATAAATAA  
AAATAAAAAATAAATAAATAAATAAATAAATAAATAAATAAATAA  
AAAAATAAGAAATGGAAGTGGATTCTTAGAAAAAAGAAAGTAAGGTGA  
TATGAGGAGATAGAGAGGATGTGGTGTGAGATGATTGGTTTAATTAGAAA  
ATAGGTTTTGAATAGAGTGGGAAAGTAGAGTTTTGGTAAATGTGGGGGA  
AGAGGGTAATGTTGTTTGAAGTGAAGAAAAAATGTTATATTTTATAAAA  
TAATGAGGAAAGTGTGTGAAAAAATAATTATTGGGATTGGGAAGGTGAT  
ATATAAAGTTGTGGAATAATTGGGGGTGGGGTTTTATTAGGATTAAAAA  
GTTATTTAAAGAATGAAATGAATTTTGTGTTGTAATTTGGGGATAAGAA  
ATTAATGTTTAGAAAGAAAGGGAAAAAATTGAAGAAAAAATTTAGATTT  
TGGAATTTAAAAATATTGTGGGTGTAAATAGGAAGGATTTTAAAGGTA  
ATTGTGAAGGGATTGTGTGGAATAATAGGGAGAAAAATGGGG

&gt;Contig2

GCATCTAAGTGGAGCCTGCATTATTACAGATTTAGCATCACCAAAGTCTA  
AACAAATTAGACTGACTAAGGCAGAACTGCCCTTATGACAGCAGACATAAG  
AAGGAAAAGGCCAAACACTGTGTTAAAAATTATCCAAATGTGAGGAAAA  
GGCAAAGAGAGTAGGTGTGCCTTTTAGTGTCTAAGCTGCCTGCCCAAGG  
GGCATCTGATGCTCTCAGGCAGGAGTCCACAAATTTTTTTTGTAAAAGA  
TCAGATAGTAAATCTTTTCAGCGTGAAGAGCATGAGGTCTCTGTACAAA  
TACTCAACCACCATTACAACATGAAAGCAGCCACAGACAACACATGACA  
AATGAGTGTGGCTGTGTTCCAGTAAATCTTGATTACAAAAACAGGCAAGA  
GGCCAGAGCTGACCCATGGGCCATAGTTTGCTGACCCCTCTGTAAAGGA  
AAGTATTTTGTGTTGACTGTGTTTACCATTGATTGAACACAAGGCTCT  
GTAAAGTTACTTGTAACTTGCAGAAGATTGATGAGTGGCAAGTAATTTT  
TATTCACCAGAAATATAAAATTATTTCTGTTAGTAGAAAAAGATAAACCA  
CTGTGATATTATGGTCTCTG

&gt;Contig3

GGGGTGTCTGTCTACCATGTGCTCGCAGTTCTGTAATAAATGTTCTCTCA  
AGATCCTTAAAAATCTCTTGGAAATTATAAAAAATATTGAAAGAGAAGAAC  
AGTTTTTAAATATATATATATATATATATTTTTTTTGGAGTGGAGTCTT  
GCTCTGCTCGTCCAGGCTGGAGTGCAGTGGCGCAAACCTTGGTTCAACCAA  
CCTCTGCCTCCCGGTTCAAGCGATTCTTCTGCCTCAGCCTCCTGAGTAG  
CTGGGACTACAGGCGCCCGCCACCGCCAGCTAATTTTTGTATTTTTTA  
GTAGAGACGAGGTTTTACTATGTGTTGGCTAGGCTGGTCTCAAACCTCTGAC  
CTTGTGATCTGCCCCCTTGGCCTCCCAAAGTGTGGGATTACAGGTGTG  
AGCCACTGCACCTGGCCAGTTTTTAAATATATTTTTTAAAAACACTTGAA  
TAAGAGTCAGTGTAACCTAGAAGTTTAAAAATGCTTCACAGAACACCCAG  
GGTTTACATTACAAGATTCTACAACAAACCTATTGTAAAGGTGAGTAAG  
GCATGTTATTACAGAGAAAAGTTGGGAGCAAACCTGTAAAAAATTATAT  
TTTTGTTGATTTTTCTAAGAGAAAGAGTATTGTTATGTTCTCCTAACCTC  
TGTTGATTACTACTTTAAGTGATTTCTTGGAGCACATGATGATCC

&gt;Contig4

GCCGTTTCATAGAAAACCTGAAAGCAATAAGATGACTAGGTAAAGCATGACAT  
TTAAAAGGTATTTCATGGGACGTGGTTACAAAACCAACTCACAACCTAAAA  
GTCTTAGGACCTCTCGCTGACTTAGGAGCCTGATCCCAACTCTGAGAATG  
ACTCAGTGTGTTACCCTGTGGCTAGTGTAGACCAATGATCCTGTCTCAGA  
GTCAGTAGCCAACAGCCCATATCAAGTACTTGAAACTTTGACTCAGAAAC  
CTCAGTGTGAGAACCTTTGACCTAGGAACCACTGTAGTGGTTAACTGCA  
ATTTGCACCCCTTAGTTTCAAGGCTTTACAACACCGGGGGCGGGAGGGGA  
AAGGCATANANCTGATGACCTAAAGGAAACCCATTGCAGCAACGCTTTTG  
TGTAAAGTGTACAAATAAGTGTGTTTTAGAAATCTCCAGGTAATGCCTT  
TGTTATTTAATGTGCTGAGACAATTCTGCACATTAAAGAATATAAAATA  
TTACCTTGTAATTCCTAATTTGAAATGTGTAATTGACATTAGACTTCTATT  
TGAATTTGAAATGTCTAAAACAATGTGGTTAAGTTTGTAAAAGGTGTGTG  
AATTTTGAAGTCTGATTTACTACATTTTTTTTTTAATTTCTTTTTTTTGG  
AGTTTTAGGGATTGCTTAGATGGCTAGAAAGATTTTATTCATCAGATTTT

FIG. 3 (1 of 52)

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TAAGTCTGCCTTGGCAGGCACCTTGCAG. JTTTGAAAGAATCAGATATATC  
AAATTTGTAGTTTAAATATTTAAGGGAACCTCAATTAAGTATGCTAGAAA  
AGAGAATTAAGTATTTAGGAGGATTTAATATGGTGTGAAAGTTGTGAAAA  
TCAAAATGGAGACACTAATGTTAAGAAAACCTGATAAATGGAACCGGG  
AAAGGCATGAAGATAGAGTTCTCACACTTGTATCCCTGATCATGAAAAAG  
ATCTGC  
>Contig5  
GGGTTTTTCCGCGTTTTTACCCGAAATCTTCAAGGGATGGGAAAAAGAAA  
ATTGCTAAAAAATCTCGGTTTTTTGGTTTTTAACAGATATTTACACNTGG  
ATCCCATTTATTATGTTGTCCCAAGGTTTTTCGGTGGGTCCCAATCAGT  
TAGCCCCCTCCACAGTGAAAGCACTTTACTTTATCACCTTCACCTAAAG  
CATAAAATCCAGCTCTTGAAAGCTGCTCCTGTTAAGTGAATATATCCAC  
ATCCCAAAGTAATGATCCATGCTTCATAATCTGCCACGGATGGATGGAT  
GGATGGATGGATGGATGGATGGATGGATGAATGGATGGATTGATTTCTTG  
GAGGATTTGTTGAATTTGGGAAATTCACGCCAGGACAGCTGGCCCAAAC  
TGCCCGCGACAACTGCTCGGTACAAGGGGAGGGTCTTGAGAGGGGTGCG  
GCCCAGCCCCAGTTTGGAAATGCCAACTTGGCTCTGCAGCCGGGCCTTA  
GCCACTTGGGTCTGGCGTCCCTCCATTATTAGCGCCATGCCGGCTCGGG  
TGCTGCCAAGTCCCTGAGAGCAAGCC  
>Contig6  
CGCGCTCAAGAAAAGCTGAAGTGTGAATGTTCTGTCTACCTTCACAGTAA  
ATGCTAAGAGAATGACCCAAGAGCAGAGGGTATCACTCTGCTACGGAGGA  
TTGATTGTAACTGGCTCTCCTGCCTTAGCAAGAAATGCCAGAACCATGGT  
CATTCAAGTTCTTGACCAAAAACCTGCCTTCATGAGAATCAACTTCCCCAA  
GAAAAAAAAGCAGAAACAGGCAAAGCTTCCAGCATGGTAGGTAATACTG  
ACCTTCTTCCCTCCTTCTTGGAGATTCACACAGTAATAATGCATAAA  
GCTTTGCCAATGGACTAAGCACTGCCAGGGGTTTTTGTATGCCTGGAC  
TGAAATGCTCTTTTTGCGTTATCATAGAATCCCAGTGCAGTCTGAGTAGA  
CTCTAAGCAAAAGGGACATTTTTCAAAAAGGCTTTAAATTGCTAGTACAA  
AGAAGGCAACAAAACCTTGCCTAAGTGTGGACAGATTAACTCACTTGGTGT  
TTTGGCTCTTTCAGTTTCCCTTGGCTGCGAAGTACTCCTGAAGCTTTCTC  
TGCGGCTCTTCTGCAAGCAGGCAAGCAAAAAACGACTGAACTTTATTT  
CGAGAT  
>Contig7  
GAAGAGCCGCTAACTTGCTGTAGTGATAAGGAATGAACTAAGGCTAGGGA  
CATATTAACATCCGCTGGTGGTGAATCTTTAGCCTAGATCTTACCCCACT  
CCTGCTCCTTCCATATGGTTTCGGTCTCAGGCTCACTACCGATCAATGGCG  
TACTAAAAGCACTAACTATAGACTCCAACACGTCTGTCTGTGTGTTTACG  
ACAAGCCGTGGAGTTAATCCCTCTGACAGTAGCTCAGATAAGGATGGGCT  
ATCATGGGCCCCGGAACCTGGGCGATGACGCTCGTCACCAACGCATGAGCTC  
CCCAAGTATGCTATACCTGTCCCTATGAAGGGCTTCCAACCTATGTGCA  
GTCCCCATGTGGAGAGTCAGGTATTGATTGATCAAGCCAGGGGTGTGGTG  
AATGGGGAGCTTCTACAGGGGTAATGATAATTGAAATGCACGGTGATGG  
GGATTTTTCATATTGGTCTCCTAAGGAGATAACAGATTGGATGCGGGGTGCG  
ATATTCCACTGCCAGGGTGTGTACCGAGGGTATCTGCAGGTGGATCTCC  
TCCCCACGTTTGATTAACTCCTGTCTTGGGAAGCATAGACGGGCGGGG  
GAAATGATGAAGGGTGACCACTCCCC  
>Contig8  
GGGAACGCAGTGCTCTGTACGATGGCCTTGATTGCCAATTCCTGCAGGGG  
GGG  
>Contig9  
GGCAAGAGATTTAATATTCATTCCATCTTCATTTGGAAGATGAAAAATTG  
GGGACCAGAGAGGGGAGGGGACTGGGCCAAGTTTTCAAAGAAAAGTCAGT  
AGGAATTGTGAATTCCTGGGGGCCGGGCCCATTAGTGTGTTTTGGATC  
AGTAAATGGAGATGTGAGTTTCAACAGTAACAGGGACATTTTAAAATTAA  
AATGATTTAACCTTTAGAAAATGTCTATTTTGTAAATGATGGATTCA  
CAGGAAGGTACAAAGAAATGTCCAGAGAGTTCNTGAGCCCCCTTCAGCCA  
GCTTCTTCCAATGTAAACATCTTGCATTATTATAGTACAACATCAAACT  
GGGAAATCGATATTGGTACTGTCCAGATAGCTTACTCAGATTTTGGCAGT  
TATACTTCCACTCATTTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTG

FIG. 3 (2 of 52)

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TGTGTGTAGCTCTATGCAATTTTATG1...GTAGCTTCATGTAACCAACC...  
AATCACAATACTTAACCTATGCCCTCATCACAAGACTCTCTCTTGCTATGC  
TTTACAGCTGTATCCTCTTCATCTCCAAACCTAAGCCACCTCACCGCC  
TCCACCATCTCTAATCCCTGGCAACCACTATTCTGTGCTCCATCTCTGTA  
ATTAATTTGTGTTAATTAATGTTATACAAATGGAATCATGAAGTATGTGTC  
CTTTGAGATTGGGCTGTTAATTTTTCACTCAGCACAATTTCCGTGAGTCT  
AATCCAACCTTGTGTGTAGCAGTAATTCTTTCTTATTATTGCTGAATAAT  
ATGCCATGGTATGGATGTATCACAGTGTGTCTAATCCTTTGCCATTGAA  
AGGAATTTGGATAATTTCCAGGTTTTGGCTATTATGAATAAAGTGAACAT  
AAGACATGTGTGTACAAATTTTGGTGTGATCAAAAGTCTCATTTCTCTGG  
GATAAATGCCCGGTAATGAAATGGCTGGGTTGTGTGGG

>Contig10

GCAAGAACACAGGCGCGTATTATAACCTTACTACCAAGACCTGAACCCAT  
ATAAAGGTTTATGCGTAACAATCATCATCCCTGTTCCAGAAGATTACACG  
TACGACCACGCTGGCTCACCAGCTCACGTGGGCCAGTACCAGAAATTCT  
CCCAAACAAACAGTCGTGTCTGAAAACAATCGCGGTGACCTCCACGGTTA  
GAAAAGCCTGTTTTCAAGTCTGGAATTGCCACATATTAGCTGGGTAAC  
TTGGGCATCACATTTACTCTCTCCGAATTTGAGATTGCAAAAACTCATTG  
GATTGTTTTGTGGATTGAAAGAAATAATGTAAATTTAGGCCGAGTGCTTT  
GACTTACGCTGTAAATCCTATCACTTTGGGAGGCCAAAGCAGGAGGGTCA  
CTTGAGCTCAGGAATTTGAGACCACCTCTGGCAACATAGTGAGATCCTGT  
CTCTACAAAAAATTTTTTTTAAATTATCCAGCATGGTGGTACACGCCTGT  
ATTCCAGCTACTCAGGAGACTGAGGTGTGAGGATTGCTAGAACCCTGGGA  
GATCAAGTCAACAGTGAGCCGTGGTTGTGCCACTGCCCTCCAACCTCAGT  
GACAGAGGAAGACCCTGTCTCAAAAAAAAAAAAAAAAAAGTAGTAAGTTTAA  
AGAACTTAGTGTAGGCCTGGCATATAAATGATATTGTTGATGTTGATGTT  
AGCTTGAAGGCACATTTATAGGAGTAGGGATTTTATAACATTATGAGCCT  
GAGAGCATATAATGTTCCC

>Contig11

GGTCTAACATGCTCCAACCTGAAGAAACCCACACTTGTCCGGCAAGGAAA  
CTACTACAGATTTCTGACCTACTGTGCAATTCGGGGCATGCGACGGGAC  
TGTGTTTTCTGGGTACGCTGTCTCAGGTTCTGTTGGGATGTAAGAATTCAA  
CTTCAGTAGTTCTCTCATAGACGCCGACGAGAGGGGCGTCTCTTTCTCT  
GATGAATCTGCGAGATCTTCCACTTCATAGAGTCTAAATCCTCCGATTCTG  
ATCTACTGGAGACCCCCACGTTACAAAAACGTCTAACGTGCGTGACAGCT  
CCCCACATAGGGAAAGATCACCTGAGTCTCACTACCTCACATTAGTGCTA  
TCTCCAGCCCCATGCTATCTACGAGATGGTCACGCGAGGTTTAAGGGGTC  
TCCGATTCCGGTGGTCCGATTACGCTAATCGTGGCCCTACGTGAACGATC  
ACTCCTGCTCGTAACATCGATACAGGGTCCGCGTGACAAATGTTACTACG  
TAGGTTCTCAGGTCAATGCCGCGTCACGAATGAGCCTAACTACCCATAA  
GTGCACGTACTGTGTTACCTTTCTGTTCCGCCAAACCTGCTACTGTATG  
CTGTGCTTGT

>Contig12

AGGCTCCATGTGCTCTAGCCTGATTATCTTTTCAAGTGTTTTATTGCTA  
ATCTATAAGGCCCTTTTCGTAAATGTTCACTCATTTTCTAATTAGATAT  
TTTTTTTAAATGTTGAGTTTTGAGAGTTCTTTAGATATTTTAGATACAAGT  
CCATTGTCAAATATGTGATTACAAATATTTTCTCTCAATCTGTAATTTA  
GTTTTTCATCTCTTAACAGGGTCTTTTGGAGAGCAAATAATTTGATTTTC  
ATAAGGTTCAAATTATTAATTTTTTCTGTATAGTTCACACTTCTAGTGT  
TAAGTCTAAAACTGTGCCTTGTATAGGTACCAAAGTTTTCTCCAGTT  
TTTTTTCTAGAAGTTTAGAGTTTCATGTTTTACATTGGAGTCCATGATCC  
ATTGTTAATTAATTTTTGTATATAGGTAGATGTTTAGGTTTAGGGTTTTT  
TTAAAAAAATTAATATGTTAATTGCTCCAGTTCCCTTTTCAATTGAAA  
AGGGTATCCTTCTCCATTGAATTGCCTTTGTGAGAAATTAATTGGACAT  
ATTGTGTGAGTCTATTCTGGGCTCTTATCATGTTACTTTTTAAAAAAT  
GCATCAGTTCTCCACCAATACCTCATGTCTTGATTATTGCAGTTATAT  
AGTAAGCCTTAGCATTAGGAAAAGTGTTTTTCTGCTTTATTCTTTNTCA  
AAAAATTTTTGGATATTCTAGGGCCTTACATATAAATTTTAAATAACT  
TTGCTATGTCTAACCGAAAGCCTTATGAAGATTTTGATAAGAATTGCAT  
TATGCCTATACATTAATTTAAAAAGAACTGATGTCTTTATTAGTTGATT

FIG. 3 (3 of 52)

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CTGCTAATCTATGAACA1,GCATCTCT...CAAAGCATTAGTCTTTCTT.  
AATTTCTGTCAATTTTTTAAATTTTCAATCCTAAAGATTCTGTATAT  
GTTTTGTTGAATTTATGCTTAAGCATTTCACCTTCTTGGTAACAATTATA  
AATGATTTTGTGTTTTTATTCCACTAGTTCATTTTCAGTGTGTAGAAAA  
GCAATGAATTTTGTGTGTTGATCTTTGTTCTACATCTTGCAACATTAT  
TGAACCTCATTTATTAGTTCTAGGAGGTTTTTTCATTTTCTTGTAGATAC  
CTTGAGATTTTCTATATAGACAGTCATGTTGTCTGCAACAGGCACAGTT  
TTATTCTCTCTTTTCAATCTATATGCCTTTTTTTTTTTTTTGCCTTAT  
TGCAGTGGCTAGAACTTCTAGCACTATGTCAAATAGCATTGGTGAAAGCA  
GACATCCTTGTTCTTGTCTTAGAGGAACATTTGGTCTTTAATCTTGAT  
TGCG

>Contig13

GCGCCTCTCTTTCTCTTCCAAAATTTCTCTTGTCTAGTTATTTGTCCAGG  
GAAATTTGAAAGCTCACTTACTGTGCAAGTCAGCAGGAAACAACCTGGGTC  
TGTGCACAGCACCTAGCAAAGTTCTGCTCTAGGAATTACACTTTGGCCCT  
GAGGTAGATTTCTACAAGAACCTTACCTTCTAAGCAGCACTGGGGTTCAT  
CTTTTCCCAGTCTCTCAGAGCCCATTTCACCTCTGAGTTCTCCCCACA  
AAGGACATTTTCAACGTTGAGTTTATTACTCAACAGAAAAATGGAATGAAG  
TCCAAGACCTAAGGAGATAGAAAGGGGACCAGTTATGGCATCTTCTCACC  
CCAGGACACCTTGCTGCATGTCTCTAGTGCTGAACAGACCCTGGCCTTG  
CTCTGTAGTTTGAATGCTCGCTGCAACCAGAAAGGCACCAAGGGGCCAG  
ACCATGCTCTCCTGTCTATCACGCCTTCAAAGCAGAATTTCCCAAACCTT  
GAGTCACAGTGCTAACACACGGGGTGCCATAACATTTTGTGATTTTGG  
CATTTTACAAAAATAAAATAAAAAAGTTAAAAATGCATTGCTCTATTCTT  
GGGGCTGGCACACTATTGCCTTTGGCCAAATCCSGTCCCTGACTGTTTTT  
TTAAATAAAGTTTTATTGAAACACAACCATGCTCTTGTGTACATATTGTC  
TCTTGGCTGCTTCGAAGCTACAATA

>Contig14

GTGTTGCTTTTTTAACACTTACCTAAAATTAATCTGTAATCCATGGATCC  
TTAATTTATTTAAAAAATAATGTTAATGAGTAGCTTTATTTTCTCCCA  
TCTAATTTAAGGCCCACAGAACACCTTCACTTACCTCAATCCTCTCCCAA  
CTTACATGCTTTTAAATGTATATATGTTAATACCGTATACTTTTAAACT  
TTCTAAAATAGCATTATTTTATAGCATGAGTGTTCATTTACATTTTGTCA  
TATATTTAGAATTTTCTTTGCTCTTCGTTTCTTCTCTATTATGACTCC  
CCTCTGGGATCATTTTCTTCTACTTGAAGTACATAGTTTAGAAGTGCAC  
TATTCAATACAGTAGCCACTAGCCATGTGTAGCTATTGAAGTTTAAACTA  
AGTAAAATTTAGTAATATTAATAAAGTCACTTCTCTCACTAGCCAC  
ATTTCAAGTGCTCAGCAGCCAGCTGCGACTAATGACTACTGTACATCAAA  
CATATAGAACATTTCCATCATGGCAAAGAGCTCTATTGATAGTGTTCATC  
CAGAGTTTCTGTTCCAGGACCAAACTGAGGGTTGGGCTGCTATTTCTCAT  
GGCCCAATAACAAGATGCAGATGAGCTGGGGAGGAAGAGAGTTTTTATTT  
CTGCNACCATTTACCGGGGAGAAGGCCTGGAAATCATCACCAGGCCAACTC  
AAAATTATTACGTTTTCCAGAGCTTATATACCTTCTAAGCTATATGTCTA  
CGTGAAGTGTGCATTCACCTGAAGACGTTAGTGATTAACCTCTTTTAAT  
CTGTAACTAAGGTCTGAGTCCGGAAGATCTTCCCTGGAGCCTCAGTAAA  
TTTACTTAATCTAAATGGGTCCAGGTGCTGGGGTAATTACCCTTATCTTG  
TCCCTGCTAAATCATGGAGGTTTGGGGATTCTTTAGAGCACCATAAA  
CTTGTTTGTGGAGGCCTGGGGGTTTCTTCTGACCCACAATAAACTTGT  
TAATCCTAAATGGGTCTGTTAAGAATTCCTTCTTTATTTTGTATATT  
TAAGGCCCAAGAAAGGCCTGGGCAAACTCTTGATGGGCTTTTGTACAT  
TCCAGCCTTTGTATAAGAACACTGGTTTTTAATATTTAACTTAACCATTT  
AGTCAGTACTGAAACAGTTGTTATAGAGATCTGCATTAGTGAGACCTGGC  
CTGCCACATTTCTTTTTCTGAAGATCTTATGGTAGTGATCACCTTTGTGA  
AAGGAAAAATAAATCTTGGGACCTCAAAATCACTAAGCCAAAGAAAAAAGT  
CAAGCTGGGAAGAATCTGACACTTAAATCCAACACTGCTAACTCATTCAT  
CTCACTCATTCATTCAATTTATTTTCTTTTTCTTTCTTTTTTTTTTT  
TTTTTTGAAACGAAGTCTTGCTCTGTCAACCAAGCTGGAGTGCACTGGAT  
CTCAGGTCACTGCAACCTCCACCTCCCGGGTTCAAGCGATTCTCCTACCT  
CAGACTCTGTAGTGGAAATTACAGGCACCTGCCACCAGCCTGGCTA  
ATTTTATATTTTAGTAGAGACGGGGTTTACCATGTTTCATCAGGCTGG

FIG. 3 (4 of 52)

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ATTCAACATCATGCTGAA.CCTTTCAA.LATCATCTTGTTTTTAGTAATC  
TCCTACCTTAACTCTCTGCTCTCTGCTAGTATGGGAAAGATGACCTGAAA  
ATCTAACCATTTATTTTTCCCCCATTAAATATCATTTTATGATTATTCAGA  
AGTTAAATAAATTGTCATGCTGCTCCTCCAAAAAGACTGAATCAACTAGCAA  
CAAATAAGAATTTTTCTCACAGCTCTGCCAGCATTTTAAAAAGAATAGCTTT  
ATTGAGCCCAGGAGGTCAAGGCTGCAGTGAGCTGTGATTACACCACTCTA  
CCCCAGCCTGGGTGACAGAGCAAAACCCTGTCTCAAAAAAGAAATTTAAG  
GAACAGCTTTATGTGTGTAATAATAGACATAATAAACAGAGCACATATT  
TAAATTGTGCAACTTATACTTTGATATAACCCTGTGAAAACATCACCACA  
ATCAAGATAGTGAATATATTTATCACCTCCTGATACAGTTTAGCTCTGTG  
TCCCCACCTAAGTCTCATGTTGAATTGTAATCCCCAATGCTGGGGGAGGG  
GCTTTGTGGGAGGTGATTGAATTGTGGGGGTGCACTTCCCCCTTGCTGTT  
CTTGAGATAGTGAATGAGCTCTCATGAGCTCCCCTTCACTCACTCTCTTT  
CCTGCTGCCATGTGAGGATGTGCTTGCCTCTTCTTTGCCCTTCTGCCATG  
ATGTGTTTCTGAGTCTCCTAACCATGCCTCCTGTACAGCTTGACAGAA  
CTGTGAGTCAGTTAAATCTCTTTCTTCATAAATTACCCAGTCTCAGGTG  
GCTCTTTATGTCAGTGTGAAAAGGAATAATATACCTCCTAAGTTACCTC  
AAGCTTGTTTTTTAATTCCTTCTCCTCCCTTCTTCATTGCCAAGCAAACA  
ACCACCTGTTTTCTGTCACTATAGATTAGTTTACATTTTGTGGGTTTTTT  
TTTTTTTTGAGACAAGGTCTGACTCTGTTGCACAGGAGCAGAGCAGCGTA  
TC

>Contig17

CGCGTTATAGGAGATGCGAACTTAAGAAATGATGATAAGGAGACTTTATT  
AAATATAAATTTGAATTATTTGCCATTACAGAAATTCTAATTATTTAAA  
ATTCTATTTCATAATTTTAACTCACTGTACTTCCCAAGCTTAGCTTAGAAT  
CCTTCTGTGCTGAGGATTAATTTAATTTGTCTTTTATAGGCCTTATCTA  
AAATCCAAGAATAATTGCCAGAATCAACCACCTTCTAAATCTGTAAGTAG  
AAATTAGTCTTTTTTAAAAATATGCATTCATAAGTATGATTAGTAATAAAA  
ATAATAAAGATGTTAGCAACCTAAAGAACATGTATTTGAAAGGTATTTCT  
TACAGATATAAAAAACAGTTTGGTTTAAATAAGAGACAATCATTTTTTGA  
AGTATGACATTTTTTGAAGTAGTTTAGTTTTATTAACCAAGAAAAGCC  
TCAAGTGAACCTTAGTCTCTGATAGCTAACATTTATTGAATGCTTACT  
GTGTGCCTGATACTTTCTGACTTGCATTACCTCACTGAGTCTCACAAT  
CTTATGAGGCTACTATTAGTAGCCCCACTTTACAGATGAGCAAATAAGT  
CACAGAAAGGTTAAATAGGTCTGATAGCTATTAAGTGACAAAGCTGAGAG  
CCTGTGATCTTAACCACTTTGGTATGCTGCCATGAAGTTAAATAGCTCAG  
TAGTCATTAAAAGAGAACATTTGCATTGAACCTTCCAAGCCACTTAACAA  
GTATATGCTTCTTAATCAATTTAATTTAGCTACATTAGATAGAATGGTAA  
AGGATCCTTAACTTAAAGTTTAAATGGAAGAAATTAGCCCTCTGAAAGAG  
GCACAGATTATTCATCTGCAATAAAAAATCTCACCTTTAGTTTTTTAAAC  
ATAGTTTTTATCTGTGTTCTGAAATGTAATAAAACAGTGCTTCTGAAG  
TGAAAAATTCTCACTGGTGAGAATTTTAAATAAGTTTTAATGATTCACCAA  
ATCACTTCAGTCATATTTCACTCATATGCATATGCATATATAGACATATA  
AGTTTTTATCTGTGTTCTGAAATGTAATAAAATAGTGCTTCTGAAGTG  
AAAAATTCTCACTGGTGAGAATTTTAAATAAGTTTTAATGATTCACCAA  
CACTTCAGTCATATTTCACTCATATGCATATGCATATGTAGACATATATA  
TGTTGTATGTATACATGACATCATTAGACACTGTGAAGGATAGCAAAATG  
TATATAAGGCAAAATTTATGAACAATGGTTTAAACGTTTGGGAAGCACTGG  
GTTACACTTTTACTTTATGCAGATTGAACCAGTATAGTATGCAAGTCTTA  
AGGAAAAATCTACTGGAAGGGCCCTCATTGAGCTTCCAGAGGCTTCT  
CTGGAAGTTGACAATACTGACTTCAGTACATCAGCTCGTAAATGAGGATG  
ATACCTACCTTATCTGCTTTACACAGTTGTAAAGTAAAAAGTGAACCTCA  
GGAAGGGAATTACAGAATTTAGGAGAACTAAAGCAGCATGTAAATAAT  
AGTCATCATATACAGTTATATAATGCTTGACAATTTATATAACACTTTCGA  
TACATGACAACAATAACTAACCCAGACATGTTTATATACATTACCTCA  
CTCAGAACCAACCATGTGAGGAAGTTGGCCATATGCTTTAATGTCCAAACC  
AGGACACTTTTGAGAGTAAAAAGCAGTACTTTTGACCAACAGGCATAAA  
TCAAAACTATCTTGTGAAAACCGGGATATATGGCATCCTTCTAGATAAT  
AGATACTTTTACTATTATTAATTTTGCTGTGAATCTAAACCTGCTCTAAA  
AAAGTTAATTTTAAAAAGTAATGAAGTACTGATACATGCTACAACATGGG

FIG. 3 (6 f 52)

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TAAATCTTGAAAACGTTATGCTAAGTG...AGAAGCCAGACAGAAAAGGC  
ACATATTACATGATTCCATTTATATGACACATCTAAAAATAGGCACATCTA  
TAGACATACAGAGACAGAAAGTAGACTAGCGGTTGCCAAGAACTGCAGGG  
AGCAGAAGATGGGGAGTGAAGTCCCAATANGAAAACGCATTACGT

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TGAATCGCAATGATATGTGCCACTTTGCACTCTCTGTGACATATATAATT  
ATTTTTTAATGCATTCATTTTTTCTCAGAGTGCATTCTGTTTGAAAACATA  
GACGGGAAATACTGGTAGTCTTCTTGTGAGTTAGAAACACCCAAACAAT  
GAAAAATGAAAAAGTTGCACAAATAGTCTCTAAAAACAATGAAACTATTG  
CCTGAGGAATTGAAGTTTAAAAAGAAGCACATAAGCAACAACAAGGATAA  
TCCTAGAAAACCAAGTTCTGCTGACTGGGTGATTTCACCTCTCTTTGCTTC  
CTCATCTGGATTGGCATATTTCTTAATATCCCTCCAGAACTATTTTCCCT  
GTTTGTACTAACTGTGTATATCATCTGTGTTTGTACATAGACATTAAATC  
TGCCTTGTGATCATGGTTTTAGAAATCATCAAGCCTAGGTCAGCACCTT  
TTAGCTTCTGAGCAATGTGAAATACAACCTTATGAGGATCATCAAATAC  
GAATTCATCCTGAATGACGCCCTCAATCAAAGTATAATTGAGCCAATGA  
TCAGTACCTCAGGGCTGCTGCATTACATAATCTGGATGAAGCAGGTACAT  
TAAATGGCACCAGACATTTCTGTCTCTCTCTCTCTCTCTCTCTCTCTCTCT  
TTTATTTATTTCAATCTTTCTGCTTGCAAAAAACATACCTCTTCAGAGTT  
CTGGGTTGCACAATTCTTCCAGAATAGCTTGAAACACAGCACCCCATAA  
AAATCCCAAGCCAGGGCAGAAGGTTCAACTAAATCTGGAAGTTCCACAAG  
AGAGAAGTTTCTATCTTTGAGAGTAAAGGGTTGTGCACAAAGCTAGCTG  
ATGTACTACCTCTTTGGTTCTTTTCTGACATTTCTTACCTCAATTTTAAAA  
CTGAGGAAACTGTGACACATATTAAATGATTTACTCAGATTTACCCAGAA  
GCCAATGAAGAACAATCACTCTCTTTTAAAAAGTCTGTTGATCAAACCTCA  
CAAGTAACACCAAACCAAGGATCTTTATTTATCTCTGATAACATATTTG  
TGAGGCAAAACCTCCAATAAGCTACAAATATGGCTTAAAGGATGAAGTTT  
AGTGTCCAAAACTTTTATCACACACATCCAATTTTCTGCGGACATGT  
TTTAGTTTCAACAGTATACATATTTTCAAAGGTCCAGAGAGGCAATTTTG  
CAATAACAAGCAAGACTTTTCTGATTGGATGCACTTCAGCTAACATGC  
TTTCAACTCTACATTTACAAATTATTTTGTGTTCTATTTTCTACTTAAT  
ATTATTTCTGCAATTTTCCCAATATTGACATCGTGTATGTATTTGCCATT  
TTTAATATCACTAGACAAATTCATCAGGTGCTACGTTGGTCCCTTGGGT  
TTACTCTAAATAGCTTGATTGCAAAATATCTTTGTATATATTATTGTTTTT  
TCTCCTATCTTGTAATTTCTTTGAGCACATCCCAAAGAGGAATGCCTAGA  
TCAATGGGCACAAATAATTTGACAGCTCTTATTAAACATTATTCTGTAAG  
TAAAAACTGAACCTACTTTTCTAGTATCACTAGCAACATATGAGTGTATCAG  
CTTCTTAAACCCCTCCATGTTAGGTCAATATGAACCTATGATCTAACAAA  
TTACAGGGTCTTATCCCACTAATGAAATTATAAGAGATTCAACACTTATT  
CAGCCCGAAGGATTCAATCAACGTAGAAAATTCTAAGAACATTAAACAA  
GTATTTACCTGCCTAGTGAGTGTGGAAGACATTGTGAAGGACACAAAGAT  
GTATAGAATTCATTCTGACTTCCAGGTATTTACACCATAGGTGGGGAC  
CTAACTAC  
CATGCACACACAATCTACATCAACACTTGATTTTATACAAATACAATGAA  
TTACTTTCTTTTGGTTCTTCTCTTCCACAGTGAAATTTGACATGGGTG  
CTTATAAGTCATCAAGGATGATGCTAAATTTACCGTGATTCTAAGAATC  
TCAAAAACTCAATTGTTTGTGACTGCGCAAGAAGAAAACCCCATGCTG  
CTGAAAGTCAGTTGTCTTTGTCTCCAACCTTACTTCTTTTACCTCTCAT  
ATGTTTGTGAATAAGCCCAATAAGCAGACNCCTCTACAAAGTGAACCTG  
GTCTCTTCTCTCTAACAGGG

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GTCTTGTAACACAGGTAAGACGAGTTCAAGTTTTATTTCTTGNTTTTAGA  
ACGGTAGTGAGCGGTTTTTCCAGCCTGAGACCACACCTAAGGTAAGTAGCTG  
AATGGGGTTTTTGTCTTGGCTAAAGTTTAAACACCAAGCTGGTCTTAATTT  
CTCCTTACCATTAGAGCACTCAGTAATCATATAAGTTGTGTGATCATTCA  
TTTGTCTTAACCTGTTTGTCTTCTGTTTTTATTGCTGTTTCAGTCTTTTTCC  
CATGGGTTTGACCTACTCTATCTGACTTGATCAAATCCAAAGGAAATTT  
CCAAATTATGGGGAATGAGGCCTCTGAAGTGGCTAAATTTCCACCCCTCCC  
ACACACACAAACGTGGTATGGTGGGGGAAAAAACGCCAGCAAAAGAAAA  
AAAAAAGGAAAAGATGTTTCATTTTGACCACCAACGGGCTTTATTTAC

FIG. 3 (7 of 52)

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ATAACAAGGCCACCTTTTGGCTAGCCAACCATACTGAAAGAGCAATGL  
TGTGGCCCCATGCTGTGGGTTCCATAGCTAACGTTCTGCCTTTTTTCCTA  
CCACGACAGCCTGGGTTTGGTTCCATAATCAAGCCTTTTCTGGTTTGATA  
CTTGGTAATGCTGAAATAGCAGCAATTTGTCTAGCTGAAATATCGTAAT  
AAGATTTTAAAGATTATTTTAAAGGACCTCAATAGTTAAAGTCAGCT  
TAATTAAAGCTAACATCCAAGATGTGTGCATGTGTATGTATGCGTCTTT  
GTATTTAAATAGCCCTCATGTTTTTTTTTCTTTCTAGGAACTTGCCTT  
TTTTTGAGCAAAAGTTTTTTCTCTCTGTTGACTGGATTCTGTTTTCTT  
CATTACTTCTGCTGTCTCTCTCTTTCTCTTGACCGTCTGCTGCATGAGA  
GCCCTAAAATAGTTTATAATAGCCTGGGGTTCTTAAAGAAAATGGAGAA  
GGTGCCAGGCTCCCTTTTAGGGAGAACTTCTATTTTTCTTATGGAATC  
CCTAGAGTGTAACAGACAAGTTCATTTAGCTCTTAACTGCTTGCCTT  
TGTGTTGTGTTACCTGATTTTTTTGACTATTATTTTTGACTAGCTATT  
GCAACAGAAGCTACTCTTGGGTTTTCAAGGAAGATTGTAGTTTAGACATG  
TAGAAATGTCTTTTAAAAAAAACAACTTTTTTTAAGTGCACTGTAA  
AAGCATCATATGGTCTAGCCTCCTAATAATTTCCCTTTTGGAGACCAG  
GATTAGAGTGGGCTTGCCAGAGCTCAGAGATCCAGTTAAAGAGAGG  
TAGTCTCGGCCGGGCGTAGAGGCCAGCCTGTAATCCCAGCACTTTGGGA  
GGCCGAGGCGGGCGGATCACGAGGTCAGGAGATCGAGACCATCCTGGCCA  
ACATGGTGAAACCCCGTCTCTACTAAAAATACAAAAATTAGCTGGGTGTG  
GTGGCAGGTGCCTGTAGTCCCAGCCACTCGGGAGACTGAGGAAAGAGGAG  
AATCGTTTGAACCCGGGAGGCGGAGCTTGCAGTGAGACGAGATGGCGCCA  
CTGCACTCCAGCCTGGCGACAGTGAGACTCCGTCTCAAAAAAAAAGAT  
AGGTAGACTCGATGTTGTGCTACCCGAGCAAGTTAGAGCAACGCCACACT  
TTGAGACGAATTTAAGAGTCTTTATCAGCCGCGGACCAAGAGACGGCTA  
ACGCTCGAAATCTCTCGGCCCTTGAAGGGGCTTGATTTTCTTTATG  
CTTTGGTTTAGGAAGGGGAGGGGAGCTCAGTTGCAACAATTCTACAGGAG  
TAAAAACATGCAAAGAAATTAAAAAGACAAGTGGTTACAGGGAAACAAAC  
AGTTCCAGGTGCAGGGGCTCTAAATCTATCATAAGATGTTAGGTATGGGG  
GCTCTGCCGGACACAACCTCAAGGCTTTATGCTGTTATCTCTTGAGCGAA  
ATCCTGGAGTAAATTTTGTATCTGCTTGTCTTCAAGAGTTGTTTCTT  
GACTCTTTGATATGTTGGGAGTCAGCGTACACAAGTTAACTCCTTGAGGA  
AGGGGGTGGGTAAGGAGTCTTGATGTCTGGTAAATGAAGGAGCGAAATC  
GAGTTCCTCTGGCTTTCTCAGCTAAGGGAGAGCTTATTCATGTGGAAACA  
AGGCTAAGTGATTAAGGGAGAAAGGGAGAGTCTGAAACAAGGTTAGGTA  
TTACAATGTCAATAAAATTTGGTCTCCTTATACAGTCTATGGTAGATTTT  
TTTCCATCTTTAATCTCCCTCTAGCACCACCAGACTTTTTCTCTCTGTAC  
CTTGAGATGTAAATTTTGTATCTGAATTTTCTGCTAAGAGTTGTTTCTT  
TTAATATGCAAATTTAGGGTTATTTAGCTGACAACTGCCAAAGTAGTGAA  
ACAAGTTATCAAGAACTTGAACGTCTAAGGTAGGAAAAAAAAGTCTTT  
ATGAATCTATAAGATGTACTTCTATTGGCATGCCTAATACGTCTATGTAT  
TTACGTGTTGTGTACACAGTTTTTCACTACTGAAATATATAGAGGAGTT  
CTAATTAATTGACTTAAGACAATAAAAGCGCTTGAATCAAATACCTTATC  
AGGAAAAAGGAAAAGACAAGTCAAATGCTTGTCAAGTCTATATAACTTA  
AGTAAATCTTTAATAAATAAGCTAGCTTTAATATTATTTGAAATGTCTT  
AAGAATTGCCAGCAGTTCTGGGTTACAGAACTAGTGGGGGTGCAGTGGG  
GTGAGGGTGGTGGGGTGGGNGGTNNNACNNNNNNNNCCCCCCCCCCCCC  
CCCCCCCCCCCCCTCCCCCCCCCGCCCGCGGGCGCGCCCCCCCCCGC  
CCCCCGGGCCCCCGCCCCCGCGGCCCCCACCCCCCCCCCCCCCCCCGC  
GCCCCGCCCCCCCCCGCGCCCCCACCCCCCCCGCCCCCCCCGCCCCC  
CCCCCCCCCCCCCACCCCCACACCCGCCCCACACGACCCCCCACCCCGAC  
GCCCCCGCCCCCCCCCCCCCGCAGCCGACGCCCCCCCCCGCCCCGCCCCG  
CCCCCGACCCCCCGACCCCCCCCCCGCGCCCCGCCCCCGCCCCCCCCCG  
GCCCCCCCCCGCGGGCGGGCGCCCCCACCCCCCCCCCCCAGCCCCGACC  
GCGCGCCCCCCCCCACCCCCCCCCAGCCCCCGCCCCCGCCCCGACCC  
>Cont1g20  
GGCAGTACGCTATAATTCCCTCTTACCTTACCTCATCTGTTCTCTGATG  
GATGTACTTTTTTTTTTAGTTTCTAAATCCCTTTTCTTTGCTCTGGAG  
ATGGGTGATTGATGTAGTCTGGGTATTGTTCCCTCCAAATCTCATGTTG  
AAATGTAATCCCCAGTGTTGGAGGTAGGGCCTGGTGGGAGGTGTTTGGAT

FIG. 3 (8 of 52)

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CATGGGGGCGAGATCCC. ATGAATAGC GGTACTGTCTCTCATAG. A  
 AATGAGTTCTCTGAGATATGGTTGTTTAAAAGTGTGTGGCACTCCCCCA  
 TTGCTCTCTTGTACTGCTTTTCGACATGTGACATCCCTGCTCCCTTCGC  
 TCTCTGCCATGATTGAAAGTTTCTTAAGGCTTCGCCAAAAGCTGAGCAGA  
 TGTGGGTGCCATGCTTGTACAGCCTGCAGAACTGTGAGCCAAAATAAACT  
 TCATTTCCATATAAATTACCCAGCCTCAGATATTTCTTTATAGCAACATA  
 AGAGTGGCTTAATACAGGCTGGGCATGGTGGCTCACGCCTGTAATCCCAG  
 CACTGTGGGAGGCTGAGGGGGGTGGAACATGAGGTCAGGAGATTGAGACC  
 ACCGGCTAACACGGTGAAACTCCATCTCTACTAAAAATACAAAAAATTAG  
 TCGGGCGTGGTGGTGGGGCGCTGTAGTCCCAGCTACTCTGGAGGCTGAGG  
 CAGGAGAATGGCATGAACCCGGGAAGCGGAGCTTGCAGTGAGCCGAGATT  
 GCACCACTGCACTCCAGCCTGGGCGACAAGAGTGAAACTCCATTTAAAAA  
 GAAAAAACAAAATTTCAAACAGAACAAAATGAAAAAATACCAAGTGAAA  
 GGCCCTATAAAAAACCCCTCTGGGGCCCATCCTCCCACCCCTCAAGTGA  
 AACCACATTTAACAATTTGGTGCATATCTTCCAAACCTTTTGTGTACA  
 CATATAAAAAACATACATGCTTTGATTGGCTCAGACTGTACATAGTGT  
 TTCCCTCTTGCAATTTTACACTTAATATATCTTTGACATCTTTCTATGTCA  
 GTGCATGTTGGCTCGATGATATTCTATCATTAAATACCCTTCCAAAAATG  
 GTAAATCATTTTAAAAAATCATTACACACAAGTACATATTTACAATTTTA  
 AAAGAAAACAGAATCCCAAAACACAACGACAAACCTCTAAAAATAATCTC  
 TATCTTTCCACCAGCATGGAACAGTTCATTCTTTTTCACATAAAACGAA  
 TTATGTGATTGGAAAGATTAACTCTAATCTACACATTTATATACAGAATG  
 TTCTATTTGTTAAGCCTATCTGAAAATAAAAAATTCAGATGATTAAATCA  
 CTTACACTTAGAAAATTAAGTCAATATACTATGAATACACATTGTGATCAG  
 TTATAATATGATGCTTCTTAGTCTAGGGTTTCAATTAAATAACAGTAAAA  
 AAAATTGGATAAATAAGACAGCTAATAACTGAAAAATCCAGAAATTCAAA  
 GATTATATTGCCAACTAAACACTGCCATTTACATTTTTTTTCTACTT  
 GGTAGCAAATGCTAATGGAATTCAATCCTGATTACTTAAAGTCAGTTCAC  
 ATCACACATTCATCAGGATAATACGAACATAATATGCCTACTATAGCGT  
 TAGATTAAGACATAAAATTTTTTGCTTGAAAGTAATGACTGCGTACCAC  
 TTGAGACATTGTCAACCACTTCAGCACATTGTTTACGAGTGACTGGATG  
 TCCACAAGGAATAAAAAACGACAGCAATATTTCTATCCATACAGATTTTGC  
 AAAGCTTCTCTCTTGCAGGTGTCTTAGCTGCTCTTCAGTACTAATCTCT  
 TTCTGCAATGAAGTCTGACTTGATTCTGTCTTGTGTACTGTCTTTCTGAGC  
 CTTCACTGGATCTGCAATCAGAACCTCAAGTGATTACAGTTGCTCCAG  
 ATGTCTGAATTTTTCTCTCCATTATTTCTTAATGTCTTTGAAACTGAAC  
 CCCATTCAATAGCTTCTTGTACCATAGGATTATGGAAGATGGTATCAAT  
 TTTCTAGTTAGTGATGGCGTTTTTTTCAGCAGTTCTTACCAGACACTCCT  
 CAAGTGAATGGGATAAATGAATATTGTTTATATATTTTCGTGTCTTCTGT  
 TCTAACAGATATTTACACCCTGGATGCCATTAAACATGTTGTCCCAAGGGT  
 CTTNCTGGGCT

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CTTTCTCCCTTTTTTACCCCATTTTTCGTAGGGATTGGTTAAAACCCATG  
 TAAAAAATCCAAACACCGGCGGGGAACGGGGGTTCAAGCTCGTATCCCCA  
 CCAGTTTGGGAACCCAAGGTGGCAGGATTGTGCGAAGCCAGGCATTTGAG  
 CCCACCCCTTGGGAAAAAAGAGAACCCCATTTTTTTTGAACAAAAACC  
 CCAACCCTCCCAGGAAAGAAATAAGTATGGCTGGGTGAAGTCACCAAAG  
 ATGGCCGACTGGCTGGTCAAGTAACTTTACCTGATGGTTCGTAGAATATT  
 TACCTTACCCAGGTGGGAGAATTGCTTGAGCCAACCCCTCAGTGTGGATT  
 CAGGAACTTGATTTAATTGGTATCGTGATTGTGGATTAGATTCTCAGGGA  
 TGCATTCACTAAGTAAAAGTGATAATAGCTACTTTAAGTAAAAATAATGA  
 ATGAATCAAACACTCTAAATCCATGGTGCTATGCTAAGCTCTTTCTGTAT  
 TTTATCTCATTTGATATTACAAATATTTGATGTGTTAATAGTAATGACTA  
 TCTCCATTTTTTACAAGTAAGGAACTGACATTGAGAGATTAAAAGACTAG  
 CACAAATCACAAAGTAAATGAGATTTGAATCCGGTCTTGATTCCAACTC  
 TACAGTATTCTAAATTCAAGGAGACTAAATTATAAGATGGAGAGCCAATT  
 TTACTTTATAACAGGGTTAGAATGGCAGAAGAGACCTGACATTACACCT  
 CTAGCCAGTGCATCATCTTCTGTAGGCAATATGCAGGAAATCTATAAT  
 AAGAACGTCCTTTGGTGAAGGCCAGGTGCAGGGGCTTACACTTGTAATTC  
 CAGCACTTTGGGAGGTCAAGGTGGGAGGGTCGCTTGATGACAGGAGTTTG

FIG. 3 (9 of 52)

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AGAACAGCCTGGGCAACAAGTGAGACCTGTCTCTACAAACAAAAACAA  
ACACAAAACAACCTCAAGAAAACCTCTTTGGTATGGATCAGAACAAAGATG  
AATTATCTATCTGATCCAAATGCTTAATGACATTAAGCCACAGTCCACTC  
ACTGCCACAATAGAGATATACCTGCCAATGCCACTCAGGTAATCCCATCA  
AAAGTGGTAATGAGGTCTGCAGCATGACTTGTCTTAGTGATCCCAGCCT  
GAGACCTTGAGATTGCAGCATTTTATTCTACATATGCACAAAACATCTGT  
TGAAAAATCTTCTAAATTGATGCAATACATTCTGATCAAGAATACCTGTC  
TGTAATCTCCATAAACCTCTCCTTTCTGTTTTAAAAAATAGTAACAGCA  
TTTCTCCTTACATGACAAAGAAATGACTTCACCATCTACGAAATAGTGAA  
TAGGAGCTGTGTGGAAGGAAATTAGCTCTACTTCTTGGTGGAGATGAGAA  
GGGAGTGTTCCTCTGAAAATCAAGGCTCTTGTTCATGCTAGGAGCCAAAGT  
CGTTTTTTAGAGTGTGGACAGTTGAGAAGATAAGACAGGGACCATCCACT  
CATGTTTTTCTTATTCATAGGCCTCTCTCAATTGGGCAAAGCACTCCAG  
ACCTTTTGGAGAGTGACACCAAGGCAAGCACCTGCTTGGCAGGCCCTCT  
CAGCTTCTACGCAAGTATAAGTGAGTATATAAAATGGGGTACTTGTGCT  
GTTGAGTACCTTATTTCCAAATGAGGCCTGCCGGTGTCCCTGTGGCTGTG  
AGAAGGCCCTCTACTGGATAGGTGGAAGTTGTGTGTTCTCATCTTTTCTAA  
CCCTGGATTGACTTGCCCAAAGGAAGCCATTATTAACACTATAATAAAA  
CCATCCTTAATCTGGGACTCTCTTCATGCAGTGGTTCTTAACCAGTGATA  
AACATGAGAGTTACTTTTGGAGCTTAAAAAAATTAAGATGCTCAAGGTCT  
ACCCAACTGACTGAATCTCCAGAGGTGAGGCCAGGGATGTATACTTTT  
GAGCCAGACCTCAGTTTACCCTGCAGAGCTCATAAGGTTGCATAACACCC  
TTTGTCCAGCCACTCTGATGAAAAGAAAAATGGTGAGGAATAAGTTTTAG  
AGAAGAAGGAGCAAAGGTGTTCTTGGCCAGTGAGAGCCAATGACAGGGAA  
ATGCAAACAATGTATCCACAAGAAAGGTAAATTACCCTATAGAGCATT  
AGGATAAATGAACATCTCATGCCTAGGGTTGAGAGAGGGTACAAAAAAA  
AAAAAAAAGACCCTCTGGATACACAACGCGATAAATGGAATAAAGAA  
TTTTTCTTGTAAATTAAAAAAATCCTTTGTTACTGAGGTATAATTTAA  
TCTATTTCTATGTATAGTTCAATGAGGTGTTATAGATAATAAATTTTTTT  
GTAAATTATTATATTGTCATATACTCATACATTCTTTTAAAAAGTCAGA  
AATGTATATAACCATTAACTTATAAATCATTGAGTCATTGAGAGATATA  
GATACAGGAGCATATTTTATATCCACCACAATAATTATTACCATCTCAAC  
AATTCATCACCCCTCAAATTTCAAGCGTAGGGGTTTTTAAATGTCAAAG  
GAGTCTACTCAGTGGGAAGAAAGTTAAGGAAAAACCTTTGGGGCTTTGG  
GCTCCTTCCCCCTGGGGTTAAAAAGGCAGGAAATTGGGCTTACCCCCCT  
GAAATTGGGAACCTGAAATTTTGGGAAGTTTAAAAA

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TCAAGCAGCCTTCTTCTTGGCTTCCCAAATTGTTGGGATTACAGGCAT  
GAGTCAGGATTCCTGGCTTAGTTTACATTTTCTAGAGTTTTGTATAAATG  
GAAACATACAGAATGTATTTTTTGGCGAGTGGGGGAGTGTCTATTTT  
TTTCTTTCCATTTCCCCCCCCCNCCCCCGAGACGGAGTCTCGCTCTG  
TCTGTTGGCCAGGCTGGAGTGCAGTGGTGCATCTCGGCTCACCAGCAAGC  
TCCACCTCCCGGTTCAAGCAATTCTCCTGCCTCAGCCTCCTGAGTAGCT  
GGGATTACAGGCGCCCGCCACCACACCTGGCTAATTTTTTTTGTATTTTT  
GGTAGAGACGGGTTTACCATTGTTAGCCAGGATGGTCTCGATCTCCTGA  
CCTCGTGATCTGCCCCGCTTCGGCCTCCCTAAGTGCTGGGATTACAGGCGT  
GAGCCACCGTGCCCGGCCAAGTGTCTTATTTCTTAACCAGCTTTTCATG  
CAATCTTTTTTATTTTACCATCTCTGTGATCCCACTCCCAAAGGTACTA  
GATGTCGATTGGTCTTAGGATCAGCTACCATTTGCCCACTGCTTTCCA  
GCCTTCCAAAAATTTTTTCTTTTTTCTTAAAGATACTCCTGTGTGAGG  
CTCAGAACTCTGAATTGCTACTGCAAAATATGAACTCGGTGATGTGAATG  
CCAGGGAATTGCCTGATTGATCAAAGAAATGTATCCCTTCTCCCTCACT  
CTTGCTGTCTTCTCATTTGTTTTCCCATCCTTGTGGATTCTGGAATTTA  
AATATCCCTTAAATGTTATAATTTTTAATGGCGTTTGGCGAAAAGTACA  
GAATTAGGTGCAAGAGTGATAGCTGTTATTTTTTTTTTGGCCTCTGAGA  
CTGTTTCATATGCAAGTTATTTAACAGAAAGTTCTGCAGTGACCTGAGA  
TGTCAGTGGGGTCTGATAGAGTACGTTTGAAGGCAGTTACTGGAAAAAA  
TAATGCCATTTCTGGTTTGTACTTCCGTAAGTTTCAGATGACCCAATATAT  
TGTTTACATGTGGCATTGAGTAAAAAAGTAGCTTCCCCCTCCTTTCTTCT  
TCCTTTTCTCCTTCTGCTTCTATAAAGCATCTGCTTTGGGAACCTCT

FIG. 3 (10 f 52)

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TAGGAGGAGAGCTTGGCCJCCCGTGGC .ATGGAGAGGTCTTGCAAGAA.  
 AAAAGAGATGCTCCCACTCAATGCAGGATGGTGTGGAGGTAAATGGGGAT  
 ACGTCTGGGCATCACTCAGGAATGGGCCTTCCTGGCAGGGAAAAAAGGGA  
 GGGGAAAGAGGAAGGGAATTNNANATNAATTGCTGAATACGGGGATTCC  
 ATGGCCCTGGATCCAGGAAGAGAACTTTGGGAGGTGTGAACCTGGAAGGCA  
 TCANCTGATGAGGAGCAGCCTGAACTCCGGGGAGGACCTGTTTTTGGTGG  
 CCGCGAAAAAAATGCCTTCCACACACAGGGAGGCCACCCGGCTGATGGGC  
 TGGGGGTGGACGGACAGCCCTAGGACAGGCTTGGGAAACCAGGCTCAGG  
 TAGGGCCTGCGAGGTTCTCGCTGCGTCTCTTCTCTCTCTGGTCTTAGAAA  
 ATAGAATCCAAGGCCTCTTGAGAGTGAAGGTGGGTTGGGAGGAGGGCAG  
 ATGGGGCTTAGGCCCAGGACACCCGTAGAGCTACTGCCAGCTGTCTCTC  
 AGGGACTCTGCTGAGGTCACTCCAAGGATCATTCTTAGCCTTGCTAGACA  
 GTACTGACAGAGGGAACCGTAGTATCGCACCCACTTCCTTCTCTTTCAAT  
 GAAAGTTTAAAGGTCACCATTTCTCTGGCAAAGGAAGTTCCACAAATAT  
 TCCATTTCCGGTCTTAGAAACAGCAAGGTATCAAGCAATTGCAAACCTCC  
 TGTGCTGGGGAATTCCAAGGAAGTAGGGGCAGAGTTCTGGTGGAGACAA  
 AGTGAATTCGAGTGAATTAGTCAGTAGCAGTAGCAGTAGCAGTAGCAGTA  
 GCAGTAGCAGTAGCAGTAGCAGTAGCAGTAGCAGTAGCAGCAGCAGAACC  
 AGAATTTCCCGCACGTGTCTCAGGCTCTCATTTGCCAACTCAGTCTCTA  
 AGTATTTTTTATGGCAGGAAAAAATAAAATAGCTATGAGTGAAATAATTCA  
 TTAGACCTGAGCCTCCATCAATTTTGTGTTTAAAGGCCTGACTCTCTTTA  
 CCTTTCCCTGGGATGGAAGATGCAAAATGTTCTGATCTCACTGTCAAAAA  
 AGAAGAACCAGTGGGTATATTGTATGCTTGAGTTCAGCCATTAGTCACA  
 AGACATAGAGATGACTGCCATGTGTGTAGACTTTCTATAGACTGTGTGCT  
 AAACCCGACCTGCCACTTCCAAGGAGTAGATGAGGAATGTCCATGGTTCT  
 GGGGAGCCCTACCCCAATTTGGGGCAGACATTCCAAAGCTCATTTTCTGT  
 GGAGGGGGTTGATGGTTAAAGGAACGGCTGGGATTTACTCTTCTTTCTAG  
 GGCCAAAGAAAATGACATGCTGCCTCCATGTTTAAATCATCCTTCCCCCTGT  
 TAATACTATGGCTTTAAGTCCCGGTTAGGGCCTTCTTCCAAAATTGGG  
 GAAAAAATTTCCCTCCCCCTAAAAATTTTTTTTTTAAAAAACCTTT  
 TTTTTTGGGGGTTGGGAAAAAACCAAAATTTTTTTTCCCAGGGGTTT  
 TTTAATTTAAATTTCTCCCCAAAATTTGTTTTTTTTTTCCGCGAAAAA  
 AAGACCCCCCAAAAAAAAAGTTTTTTGGCGGAAAAAAAATATTTTT  
 TTTGTGTTAAGAAATGGAGAAGAAGGGGGTTTTTTTTTTCTTCTCCCC  
 CACCCGCCAAAGGAAAGGTTGTTACAGATTGTTTTGTGTCTCCCGCCCA  
 T

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ATGTGCCTGCGAAATCATCCTTCCAGAAATATTTGCCCTTTCTTTTGT  
 ATAGAGTGGCACTGCCCTATATGGTGACCACTTGCCACATGTGGCTGTTG  
 AACACTTGAAATTGGCTTGTGAGAATTGCAGTGTAAAGTGTAAACACAT  
 ACCAAATTTCAAAGACATGGCACATAATAAAAAATGTAAATATCTCATT  
 AACAATTTTATATTTGACTGTGTAGTAAGTAACATTTTGAATATATTGGATTA  
 AATACATGGATGATGCCCAACACCCACAGTCCCTTATCAAGTCTCTACT  
 TCACATTTTTGTACTTCTGACTTAGAAATAGCACTGGCGTCTAAGAGCCT  
 ATTAATGTGCTCAATAGGTTCTTGGGAACCACAATTTTAAACAAAATGAC  
 ATATAAGAAAACGAATAACATTGAACAAAATGACATTATTCGAGGACCTG  
 CTGCATGTTGTTTCACTTAAAGTCAGTGTCCAAGAACTATCAGTGACAT  
 TTAGTGAGGAATTGCTGTCTTCTGTTTACAGGAACCTGGGCAAGTTAC  
 TTAATTCCTCTAAGCCCGGTTTATATCCCTGCAAAGAGAGAAGGATAATA  
 ATCACCAGTACTTAGTGATGTGTAAGGAGAAAAATAAAATAATAAATATG  
 AAATGGCTGACAGTGTCTTGTGACACAGAAGATGTGTGATCCACAGTAG  
 CTGCTATTGTCTGCCTCACTTCACTAGTAATGGTCCAGGGAGGCCTTTAA  
 TGTGCATGGTGCAGTACATTACATGTTGGACATGGGTGAAGGAAAGAC  
 CAGGCTCATCTAAACACAATAGGATGCTTGTGGTGTTTTGGAGGGAATC  
 AAGGACTAGTTATCCACAGCTGTAACATGCATGGATCAAAAGAGATAAGG  
 CACACAAAAGACTTTGTGAGTACAAAGCATTACAAAATGCAGAGACCAG  
 CTGTGGGTGGTGGTGAAGTACAGCCAGCTTCCCTCTGTGCTGGCTGAGT  
 GGTTCTGGGCAAGTACGCCATCTGTCTTGATGCCCTTCCCATCTATAG  
 AGAGGGAGCAACTGAGGCCCTTCCAATACTGAAGTCCTTTATTTCTGCT  
 ACTTTAGAAATATCCACATTTTGGTAAATTCAAATGATCCAATGATTCC

FIG. 3 (11 of 52)

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ATTTCTTAATGTTCAAAA CAGCCCCA AACATCTAAATGAATCAAAAC  
AATAAAATATTTATGTGTATGTTTTGATTGCTGAAACTTCTATTTTAGC  
AACACACACACACACACAGAACCCATAAGCCTTCATCTTTCTTGAT  
AAACGAGCCTTCTGTCTGGCCATTTAAGTCACGATTAAGTAAATGATTT  
CCAACTCGCCTTTTGCAGCAGTTCAGATGGGTCTTTCTGCGTGGCAGTG  
GCCCTCCTGACTTATGATTTCTGTGTGTCTGGCCTGTTACCACTGCAGCT  
TAACTGAGGAAACAAGAACAAACAGCCTCTGACCCCAAGAGACTGTTGG  
AGGCAAAGGCTTCAGTCCCAAGAACCTCACACGTGGGGAGCCCCGAGAGCC  
CAGCCCTGACCTTTTCTCCAGTAATAACATAAGAAACAACAGGCACTGGC  
CTTATTTTGGATACAAAGAGTGGTGCTTTTCTTAAATCTTCTTTAGTC  
AGGGGTACCCCTTCATGGACGCCCCAACATCCATGGTTCTGTCTGAGTC  
CCTGCTTCCATATCTCTGCACTTCTCACTTGAAATATCCCTGGAGTACGT  
TAAGCAGCCAGGTTTGGAAAGTTCTTGCTGTGCAGGCGGGTGTGTGCATGT  
CCTCTCTCTCAACAGGACACAAGCTCCCCAAATCAGACGGTATGCCTCCA  
CGCCCTTCCCAAGCCTCCCCAGCAGCACCGAGCATGTGAGGGGAGCTGG  
GGCCAGGCCATGATGGGAAGCACTCTCTGCCTAAAGACTAGGGTGATGC  
GCCCTCAACTGTGGGAATGAGCCCCAGCTCTGGTGTCTGCCTCGGTTTTT  
CCTCCTGGACAATCAACATGAACTCCTCAGCCCTCTTATCCACTTTGCAT  
AAACTGAAAATAACAAACCCAGGGTCTTTCTGTCAAGGAAAGGGTTTTT  
TTTTATAAGATTAAACAGAGATGATTCAACACACCCAGGATATAACACAT  
GGGCCATGAGTCAAGGCCAGGCATTGCTCTGGTCAGCCTGTTGTTTGGGC  
CCCCCTTGGCAGGGCTCTCCCTGAATCTTCCCCCTCTTGACTCCCCATCA  
CCACAGCACGTCAGCTTTGGGTACAAGGCCAGTAAATGGGGAAGGGGGT  
CAGATGACATAAAGAGCCCTTTCTGTCCATTGAAATATATTTGGATAA  
CAGATGGCATTTCCTCTGTGTCTTGCCAGGGCCAGAGCCTCCACTTG  
CTAGAGGCAGACAGAGGATGGAGAGCCCTTCATTAGTGGGAGGACATCA  
CAGGTGGGCAAGAAACCACAAGCTTGCACTGAGGCCAGCCTTGAAATAG  
CAGCACCTGCCGGCAGCTGTGGTCTGGGGACAGGGTCACAGGATGGAGGG  
GCCTCCTAAGCCTTTTATCTCTATGTACTAAGTACAACCCATTTCCAC  
CTCAGAGAGCCAGATCAGCCTCTGTGAGGTCTGGTGGCAAAGGATAAT  
TGCTTGCCCGCTGCCCCGGTGGGTGCTTGTGCTTGCAATTCCTGGGAA  
GGTTGTTGGGTTACTCTGCAATAGGTCTCTCTGACCAGCTCACCTCCTA  
CTGCAAACCTCAAACCAACTTCAAAGAAGATCCAGCACC

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CGCGTAGTCTAAAGACTGAGTCTGAAGCTGTCCCTTCTGTCTATGGACTT  
CAGATTTTAGCCCACTTGAATTGCTCCATATCCTCCAAGCCATGGCCATC  
CCTTGACTCTCTGGGCTCCCAAGCACTTGCTGCCTTCATCACACAGTTTG  
AGTTAAGGCAGAAAGACTGGTTTCCATGTACACTTGTGGAAGCTTCTC  
ATTTCTTTATATAATCTCTGTCTTTGTCTACTGCTTTAAATCTAGAAA  
TTGTTTACAAACACAAAGGTGATCCTTTAAAGCTCAAAGCTGATTGTGT  
CACCAATATATACCACTCTTAATGGCTTCCATTAACTTTGAGTAAAGA  
TTTTATGGAGCCTACATAAGGCCATGACTACCTGGCTCTTATTTTCTCC  
TCATCCTCATCTCACCACTCACTCTCCACTCCTATACCCCTCACTCCTT  
CCCCCTCCTCTCTGAGCTCCAGACTCCCAATTACCTACTTCCACCCTT  
TTTGACCCCCAGGGACTTATCTCAGCCTGGAATTTTCCCTCTTGCTCTC  
CACTGAACTGTCCACTCCAGTCTAAGACATGTGCTTATGTCACACGCCC  
TTACCGTGCTTATCTCAGTTTGTAATTATCTACTCATTTAGAAAAGTGT  
GATGAAGGTCTTCACTGTGAGCTTTTCAAGATAGCAGGAATCATAGCTGAT  
TTTACTTACTTAAAGGGGTTTCACTCTTTGTAATTTTTTTTTTTTGGAG  
ATGGAGACTCACTCTTGCCAGGCTGGAGTGCAATGGCATGATCTCGGCT  
CACTGCAACCTCCACCTCCTGGGTTCAAGTGATTCTCCTGCTTCAACCTC  
CCGAGTAGCTGGGATTACAGATGCCTGTCAACAGCCAGCTAATTTTTT  
GTATTTTTTGTAAAGACGGGGTTTTCATCATGTTGGCCAGGCTGGTCTCGA  
TCTCCTGACCTCAGGCGATCCACCCACCTCAGCCTCCCAAAGTGCTGTGA  
TTACAGGCATGAGCCACGGCACCCAGCCACTCCTTTTTTACTTATGGGTG  
AGAAGCCATTAGAGATCATTTCTTCTTTCTTCTCTTCACTAAGGCA  
CCAGGGTCACTAAGTAGTAGGATACTTTGAACTAGAACTCAAGAAATTGA  
GTTTTAATTTTACCTCACACTCTCATATGAATCTCCATGTGACCTCGGG  
CCATACTCCCTGTACCTGTTTCTCTTTTATAAAAGTAAGAGTTTAA  
ACTAGATGGTCTCCGACATGCATCCTTCTTAACATATTCTGGAACCTTC

FIG. 3 (12 of 52)

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AATAAACTAAGATAAAL AGAATAATTAAAACCTTAATTTAAAAGAACAA  
GGAAAGGAAGCAGTTACATTAAGCAAAAGAGACATCTTCATGGTTGAAGA  
AGTGTATGCCCTGGTGTCTGGATCCCATTAGGAACTTGGTAACCTTGC  
AATCTTGGGCAGATTGCTTAATTTCTCTAGACCATGACTTCCTCTTCTGT  
AAGATGTGATAAGAACATCTACCTCACAGGTTTCATGAGAGGATTAAATG  
AGATAATGTATTATAATCCCTTGAACATGGTAGGCTGTTATGTAAAGTCC  
TTTCCTCCTTCTCTGTAGCTATCATGGAATTTAAAACACATTATAACTA  
GAGCATGAGTTGCGACTAAAGGCTCAATTGTCTCTGCATGTGTTGGCTCA  
TGCATGCTTTATTCTCTGAAGAGCTTTTATACCAAGTGAAAGGAAATAA  
TTGCATTTCCCTGAAAATTCACAGGAAAAAGTTATGTTTTCTCTTCATT  
CAAGTGATTCTGTAGACCCCAACCATGCAACAATTTAAAGTTGCTTC  
CAAATATATTTACAAATATTTCTGTCTTCAAGGAACAATGGCAAGACCA  
TGACTCAGGTTACATCCGGATTCCACCACTAACCATGTACCCAATTACT  
TCAGTCACCTTCATTACAGGCTTACATATCACAGAATAAAATCAGATTC  
ATCAGAGGAGGTGAAGACAGGGAGAGGAGATATTTCAATCCCTTCTCCGC  
AACCCCGTTTTTTTTTTTTTTTAAACAAGGATCCTAGAGTTACTGAATG  
ATAGCAGCTTTGAGGGGAAAGACCCTAAGGATGATCTTTATAAGCCATC  
ACTTGGTGTGGTGGTGATAAAAAAACTCGAGTATCTTTATGCAGTGGAAA  
GAGAAGATTGGACTCGGAATCAGAAGCTTGAGTTCAAGCACTGGTTTCAT  
CAGTCTTGTGATCTTGGGTGGTCACTTAACCTCTTCAAGGGTCTCAGC  
TGTGAAAGAAGATAGTATCAGCTAATTCTTGATGTGCAGTGAGGAGGCA  
GTGAGATAGTGCAGGTAACTATAAAACAATGTGCATGAAACGCATCA  
CAGTGATCTTTGGACCCACAAGCTCCAATCTTATAAAACATATCCAGTC  
ACCCACCAACATAGATCATCTACCTTGCATATCTGATTTTGTGGATCAT  
GGGGA AAAACTGCTGATTCTTAGCAAAAACCCATGGCATAGGATAAGTGCA  
CAATAATTTTTTTTTTCTAAATGATTTAGATGACAGTGACTCATTAAGGG  
TTTCCTGAGGCCTCCTCAGAGTCGAGAGGTGGGTGCCTGAAGCCACCCAA  
AGTCCCTGTACAGGATGGCTCCCAACGCACACACCACAGGCCTGCCAG  
TATGTTCCACTATCTACCCAGTAGAGCCCTGCCAGTACGTTCCACTGTC  
CCTTCCCTAGAAGAGGTGACTGTTGTTACAGTCCCAGAAAAGCGGGCTC  
CCCAAAACAATTGCAAGGACCCACCTCTCTGAACTCACCACCCCTAGT  
TTTCCTTTAAAATCAATTTACAAGAAGATCATGTGAAGGAAAAGGTTGG  
GTGATATTCTAACCCAAGTTAGCTGTTTCTCAACCAAGTTCTCTTTGAAA  
AATTCACAACACACCTTTGGGGAATTATTTACAACAGAGGAGTGAGGATG  
GGACCAGGATAGGTATTGCCTATGTTGGTGGAACAGGGTTTTTTTCTCTG  
GATTACCAAAGAGATGGTATGCATTGCTCCAGAAGCTAAATATCTTCAG  
GCTTTCATGGTGGCCTTCACCTGAAAATGTTATCCCTGTTGAAGCTTTC  
AAGCCAGTATTTTATAAGAACTATATTTTCTTTGGTGAAGTGAAGCATT  
ATAATGATGACTATACAGGTTCTTGAGTGACTGAAGCCATCATTAGCATT  
GTCATTATTTTTGTTTAGTTGCATCTCCATAGCAGCTCACATTACAATG  
TGCTTTGCAATTGTTCTTAGCAATAGCCCTACAAGATTCTCAGGAGGA  
GAGGGTTAATCCGGATTAACATTTCTGTGAAGCCTAGCGAGATTAATCGC

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AAGAGTTTTAAAATTAAGTAAGGACGCCGGGAAACAAATCAATCCCAGCA  
AACATTTTGTGGGATTTATCATTCAAGCAATTTTACAGTTATCCCTGTC  
AAATACATTAAGTGTTCAAAATTGGGCATAGGGGGAACAAAATAATAAAC  
CCAGCCAAAACAGAATAATCCCTGTTTGTTCATGTTGGATAAAAAAGAC  
ATTACTATTGGTGTAAAGGAAATTAGATACATCTTCATTATTTAGTAAAA  
TTACCATAACTTCTAACTTTGTGGCTTTAGGCAGTCTAGTCCACAGGCAG  
GAAGGAGGTTTGTGTTGGCAAATGACTGTTATCATCTTCTGTTTCAAAGC  
TAAACCATAACTAAGTTCTCCCAAAGTTAATTCAGCATATGCCAGGA  
ATGAACAAGGACAGCCTGGACGTTAGAAGCAAAATGGAGTCAGGTAGGTC  
AGATCTTCTTCACTGTCTCAGTGATGGCAGTTTCATAACTTTAAATGATG  
GCTATCACAGTTTTTATAAATAATCTAGATAAACAGTTAAAATAAAATAA  
TTAGGTAAATGTAGTGCGATAAATATTAGTAGACAACTCACCATAATTT  
AGAATCTAAAGTTAAATTAATAATAATATTTTATTATTTGGTATTTTCC  
AAGAAAAACATATTGTAGGAAACCATTCTTTTAAAAAAAAGTGTCCT  
TTTAAAAAGGTGAATAATTTTTGTCTAATTCAAAGTTATTGAAAAGTTA  
TGTATAAAAACAGGTTAAAGGAACAAGGAAATAAGGAAATGTAAAGAAA

ATTATAGAAATAAAGTGCATTTTTTTGGTAAGAAAGCTTAAAGAGAAA  
ATTTTAGGTAAGAAAGAATCTTACCTAAAATTTTGTGCTAGAAATAAAGTG  
ACTGGCTAAGAAAGGGATGTTCAAAGCTATTTATGACAAACCCACAGCCA  
ATATCATACTGAATGGGCAAAAGCTGGAAACATTCCCTTTGAGAACTGGC  
ACAAGACAAGGATGTCCTCTCTCACCCTCTATCAACATAGTATCGGA  
AGTTCTGGCCAGGGCAATCAAGCAAGAGAAAGAAATAAAGGGTATTCAA  
TAGGAAGAGAGGAAGTCAAATTTTCTCCGTTTGAGATGCATGATTGCAT  
ATTAGAAAACCCCATCATTTTCAGCCCCAAAACCTCTTAAGCTGATAAGC  
AACTTCAGCAAAGTCTCAGGATACAAAATCAATGTGCAAAAATCACAGGC  
ATTCCTATACACCAATAATAGACTAACAGAGAGCCAAATCATGAGTGAAC  
TCCCATTCACAATTGCTACAAAGAGAATAAAATACCTGGGAATACAACCT  
ACAATGGACATGAAAGACCTTTTCAGGGTGAAGTGCAAACCACTGCTCAA  
GGAAATAAGAGAGGAAACAAGCAAATGGAAAAACATTCATGCTTATGGA  
TAGGAAGAATCAATATCGTGAAAATGGCCATACTGCCCAGTAATTTATA  
GATTCAATGCTATCCCCATCAAGCTACCATTGACTTTCTTCACAGAATTA  
GAAAAAATAATAGCCAAGACAATCCTAAGCAAAAAGAACAAAGCTGGAG  
GCATTGTGCTACCTGACTTCAAACCTATACTACAAGGCTGCAGTAACCAA  
ACAGCATGGTACTGGTACCAAAACAGATATATAGACCAAAAGAACAGAAC  
AGAGGCCTCAGATATAACACCACACATCTACAACCATCTGATCTTTGACA  
AACCTAACAAAAATAAGCAATGGGGAAAATAATTCCTATTTAATAAATG  
ATGTTGGGAAAACCTGGTTAGCCATATGCTGAAAACCTGAACTGGACCCCT  
TCCTTACAACCTTATACAAAAATCAACTCAAGATGGATTAAAGATTTAAAC  
ATGGCTGGGCATGGTGGCTCAGCCTGTAATCCAGCACTTTGGGAGGCC  
GAGATGGGTGGATCATGAGGTCAGGAGATGGAGACCATCCTGACTAACAC  
AGTGAACCCCTGTCTCTACTAAAAAATACAAAAATTAGCTGGGCATGGT  
GGTGGGCGCCTGTAGTCCCAGCTACTTGGGAGGCTGAGGCAGGAGAATGG  
TGTGAAACCAGGAGGTGGAGCTTGACGGGAGTGGAGATCACGCCACTGCA  
CTCCAGCCTGGGCAACAGAGTAAGACTCCATCTCAAAAAAAAAAAAAA  
AAAAAAGAAGGATTTAAACATAAGACCTAAAACCATAAAAACCATAGAA  
GAAAAACTAGCAATACCATTCAGGACATAGGCATGAGCAAAGACTTCAT  
GATTAGAACACCAAAAGCAATTGCAACAAAAGCCAATTGACAAATGGGAT  
CTAATTAACTGAAGAGCTTCTGCACAGCAAAAGAACTATTGTGAGAGT  
GAACAGGCAACCTACAGAATAGGAGAAAATTTTTCAATCTATCCATCTG  
ACAAAGGGCTAATATCCAGAATCTACAAGGAATTTAAACAAATTTGCAAG  
AAAAAAAAACCCATCAAAAGTGGGCAAAAGATATGAACAGACACATCTC  
AGAAGAAGACATTTATGTGGCCAACAAACATGAAAAAAGCTCATCATCA  
CTGGTCATTAGAGAAATGCAAAATGAAACCACAATGAGATACCATCTCAT  
GCCAGTTAGAATGGCGATTATTA AAAAGTCAGGAAACAACAGATGCTGGA  
GAGGATGTGGAGAAATAGGAATGCTTTTACTGTTGGTGGGAGTGTGAG  
TTAGTTCAACCATTTGTGGAAGACAGTGTGGCAATTCCTCAAGGATCTGGA  
ACCAGAAATACCATTTGACCCAGCAATCCCATTAAGGTTATATACCTAA  
AGGATTAGAAATCATTCTATTGTAAAGACACATGCACATGTATGTTTATT  
GCAGCACTATTCAATAGCAAAGACTTGGGAACCAACCTAATGCCACC  
AATGATAGACTGTGTAAAAAATGTGGACGTATACCCCATGGAATACTAT  
GCAGCCATAAAAAAGAATGAGTTCATTCTTTTGCACGGAAGTGGATGAAG  
CTGGAAGCCATCATTCTCAGCAAACTAACACAGGAACAGAAAACCAACA  
CTGCATGTTCTCACTCATAAGTGGGAGTTGAACAAATGAGAACACATGGAC  
ACAGGGAGGGGAATGTACACACCAGGGCCTGTGAGGAGTGGGGGGCAA  
GGGGAGGGATAACATTAGGAAAAATACCTAATATAGATGACGGGTAAATG  
GGTGCAGCAAAACCATGGCACATGTACACCTACGTAATAAACCTCCAT  
GTTCTTCACATGTATCCAGAACGTAAAGTAAATTTAAAAAAGAAAGAA  
AGAAAGAAAAGGATGTTACAGCAAAACAGAAAGTCCAAGCATGTGATGA  
ATAGTCTGTGTAAGTCACAATAAGAGGATTTATTTAAAAAACTTTTATA  
TGATAAAGTTGTCTATAATTAAGGGAAATTATAATGGTCTTTCTAGAGA  
TTGGGTTGATGTTAAAAAACTACTTATATATTA AAAAATTTGGTTAGAACA  
ATGAAATTTTCTACGGGGTTGATTCACTCTTAATAAATTATAAGAGACT  
TAAGAATTTTTTAAACCAAAGTTGAGCTTTTATTGCATCTTGCTGTT  
TTAGGTTTTCTCTCCCTTTTAAAGGGTGGGAAATAGTAATGCCCTCCTT  
CAACTCCCTTCAGCTCATATACGTTTTTTACCCTCAGATTCTGTTGTG  
TGTCCTCATGCTAACAATGTTTTCTTAAAGGTCTAAAGGAAATGTTTTCT

FIG. 3 (14 of 52)

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TCCAACATAATATTCTGTCATTGCAGAAGGTCTTTTCTTTTGCCTTTTG  
GTAAGTGGCTTAACAGATTTTATGTTTTATTGAAATAATTTCTATGCCAT  
TATTATTAAGTTTTGGTTTGCTTAGAAAACACTGAGATTAATACAATTTT  
TTAAAAATTATGATTATTACATCCATATATCTTTATGTATGTGCTTTAA  
AGTCCTTGTGACATTGAGTTCTAGGGCTTGACTCCTGGGTCTTAAAAGGA  
CAAGTCCTGCTAAATCTTAAATACTGACAGCAATTAAGGCTCATCTTCA  
GGACTGGTAGAAAATGCCAATCAAATAAACTGCATTCTTGAAACACAGA  
GCCAGAAATTAAGCTATTCAACTCAAGGCCAGGAAGTATAGTGGAAGA  
GGTGGGTGTGTGAGATTGTAAGGGCCAATTTGAGAGATAAAATAAGTTC  
AATTTCTCTATAAATTAATCATATCATTGATGTCCAAGCCACACTGATG  
CAAGATCAGCATATGGGTCTGTGTGAGATTAAACAAGGTTTTCTTGAAGC  
ATTAACCTACTCCTTAATAAAGGTTATAGAGGTTATAAAAGGCTTCTGGA  
AGTTATAGCTATGGTCAAGATAAAAATTTATAGATTGTTAATACAATTT  
TGGAAAACAAATTTAATTGGCTTCTTGCTGTTTTTATTAGGGCTTATTGT  
TTGGAAAATTAAGTCTCGTCTCTCAAAGAATGAAGGCTTTCACCTTTTTT  
TTTTTTTTTTTAACTCTGAGTTATCACTTTGGTCAAATGAATGACTTA  
TTTTCAATGACCTTTTCAAGTGTTTTAAACCTTTCAAATTTGACAAA  
CTTTCCAAAATCAAACCTACAAATTATGTCTTTTTATGACCTAATGAATCC  
TTAAAAATACTAGGTTCCCTAAAGTCCAAAAAATAAACATAA  
TGTGGCTTATTTGGTATAAAAATTTTACAAGAAACATTGTCAAATATAAA  
ATATTGTGTGGTTTTGTTTGGGCTGTATTTGTATAAATATGTTAT7GGTA  
TGTGTTCCAAAATTATAGGAACTCCTATAATTCTGATATGACTTGGTGT  
ACATTATCAGTAATAATTATAATTGTTATGGTAAATATTGTGTGCCATG  
GAGGTAACAAATTTCTCATCAAGTGTGTCTTTGACTATGGTTGCCCTAA  
AAGTTTTGGCATTTCACAGACAATTGTCTTGGTCTTCTTTAGAAAG  
GTGGTTTTATAATCAGCTATAAACTCTAACGGGTGCTCTTGAATGCAGG  
CTTAAGATAGCTTTGGAGACTGTGACATCAGAATAGAGGAAAACTTTCA  
GTATTCATGGAGTGTGAAATATTATGAATATCAAGCAAAACAGGAATT  
AACTTCATAGATGGAAGTAAAGAATGCTGAAGTAATCTTTTGAAGTTTT  
TTCTTAGAATGTTGATCCTTCGTTTTGTTTTTCAGAGTCNAGGAAATTT  
TTCTGTTGAGATATTGACAGCTTTAACAATTAAGTATACTCCAGTGAACA  
CAATTTGGAGCA

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ATCTAGTCATTCCCCAGCCTGACCAATTCAATGGCCCCCATCTTAGTTAA  
AATTCCTCACCCTGACAAGGCCCATCTACGCCTCTGACCTCATGCCCTC  
CACTCTCAGTCTTGCACTCACCCTGCCCACTCAAGGGCTTCCCCAGGTT  
CCTTCTTAGATTCCACCGATAGCTCAGGGACTTTGCACATGCTACGGTCT  
TGCCCTGGCTCCTCCCCAGATCTTCTCATGCCTAGCTGCTTCTCATCAGC  
ACCCCTCAGAGACTGTCCCTGCCCCACCTCTCCAGGTTCCATACCTGCCA  
CCCTCCCCCAATCACGTAACAGTTTTCTTCACAGAGCGAGTTACCATCCCA  
GTATTTCCCTAACTTATTTTTTGTGACTGGTCTGTTGCCTGTCTCCACCA  
CAAGAACATAAGCTGCATGTGAACAGGAGCCTTGTCTATCTTGTCAACCC  
AGTGGCTGTGACATAACCTGATACACATTAGATGCTCAATGATGTTTGAT  
GAATGAAGTGTGGTAGTCCAAGTGTGTTTCTTGTCTGTGTAAGTATGT  
CTGTTGTGGTTTCTTAAGAACCTACAGCTCTCCACTGTGACTCCTGTTT  
TATGGTCTGATTGCTGGACTAGAATCCTAACCTACATGCTTACTCTTA  
GTGTCCTCCCCAGAGGCTGAATCCAGTCCCTAAACCTCCACCAAATGG  
CTAAGACCTAGCTTCCAACCAGACAGGCCTACGCTGAGACCTCAGCACCG  
CCCTTCTGCGGTCTCATCTTAACGCATCCTTCAGGGCCCAGCTTAAATG  
TCTCTTCTCCAAGGAAGGCTATCCTCTTCTGCCCCCTCAGTGCTCTCCAT  
GCCTCCTCTATGCCTCCATGCCTGCTTTCAACCTGCAGAAGTGGAGAAA  
TTGCTAATCTGCTGTGTTGACACTGTGCTGGGGTGCCTTGGGCCAGGGAG  
CAGGCTGGTGGTGTGCTGATAGCCCGTGGCTGTGCCAGGTCCATGCTCA  
CTTCTGAGCCCCAGTGGAGTAGGCTCCCTTTCCCTTATTGCAGCACTCA  
GAGGAAGGACGTGCTTCTTAGGACAGATCTGGCCAACCTCTCCCTCGTGA  
GAGAAGGCCCAGCCATCCTCTTGCCCTCTTTCTTCTCCTGCCCCCGAGT  
AATAAAGGTGCTGTGCTAGAGCCTTCTAGAAGGAGACCCAAACATCCACC  
ACACATTCCAGTTCCAACCGTCATCCACATGGCTGGCTGTGCAGGTAAA  
CGCAGAGTCTGTTTACACACCCCAACCATCTAGTATTGGATGGGAGGACA  
GTAGCGTGACACTCTTCTCAGCCTTGAGCCCTACTGTGGGCCCCACCCA

ACCCAGATACCAGAGGAGCCCTGTACTGGGATGCTATTGGATGCTTGTCC  
 AGTCATGTACAAAGTTAGCCCTTTGTTATATAGAGTTAGCTACGTACATC  
 TTCCTCTGTAGGGAACCCAAGAGGGGAGAAGAGATATGTAGTAGGATTTA  
 ACCTGCAAAATCCTCTGCTGAGCACCCTGCACTACATACAGTGGGTAGCAT  
 GTGGTAGGTGCTCAATAACTATTGACCGATAGATTGAATACAGGTAGGAT  
 GGTGACACAATCTAAGATCCCAGGGGTGGGAGACCACACGCTTGTTAG  
 GGAGACCCAAAGTGGACCGTGTGGCCAGAAGAGTCCCGCACTGCACTCTA  
 GTGACAGTGCAGAAAGTCACTGTGGGAAATCTAGAAGTTTCTACAGGTTG  
 CTATTTTCATCATAGCACTGTGCAGGCCAACCTTCTGCTCCACTGGCTG  
 TTGGGAAAAGCTTTCTCTTTTCTTCTAGCCAGGGAGCTCTCAAAGTGT  
 CCACCTCTCTCACCTCCACCCAGGCGTCCAGGTGTGGAGGACACTTGCCGG  
 CTGCTTGTCTGCTGACTCATCCCTTGGTTTCACTTGGAAAACCTACCACC  
 AGCTGGCCTCTTTCCAAGCATCAGCCTCCTCATTTTCTTAATCCCTTAGG  
 TGTGATCTCACCTCCACACAGTAGATTGCCTCAAGGCCCAATTCCAATAT  
 GAATAAAAAATGATTATTTTGTCTCTTCCAATCTTCTTTTAAATATTA  
 TTTTATAATTCCCTTTAGGAGGATCACCTAAGTGAAGACTATTTTACCT  
 AAGAAATGTTAAATGTAAAGACATGGTTGTAATCTGGGGATTCTGTTA  
 AAATGCTAGCAGACAGAAGTCAGACGACAGGCTAGAAATGTGTGAAGAG  
 TGGTTGCCCTTTGAAAGGCGGAGTTGGTAATGATTTTCTTCCATTTTCCA  
 TGCTTTCCAATTCTCTACAAAGGCCCTTAATATTACTTCGATAACCAGGAC  
 CTCTGATAACCTGCCCCACCGAGTAAAGACTTAGCTGGGAAAGTCAGCT  
 TCATGTGAGGTAAAGGAACCCAGGTAATACACAATTCCTCACTGCCAACTG  
 TCGGGTGTGCAGGCCTGAGCTTCTGCTATGTGGGAGGAAAGAGAAAGAAG  
 AGAGAACTCCAAGATCCAAGAGATCCAGCAAGAAGGCTGGAGTCTGAGG  
 ACGCAGAAAGCTGAATGGCACAGTTACCACTATTGTGCTGAGGTTCTGTG  
 GCCTCTGGGTCTCTTGACAACCTGGGCAAAGACCCACAGAAAATCTCTCT  
 AGACCTACCTGTGGGAGGGGAAAGTGCTTAAGATCATTTACAGGACAGC  
 CACCTGGACCTCAAATGGCTTACAGTTCTTTCATCCAGAGGGTCTTCATT  
 TAGTACATACCAGGTGCTAAGCTGGGTGCTGGAGACATGACGGGGAACCC  
 ATTTACCATGGCTTTGTTACTGTGACATTACATCTAGGGAAAGCCAGCA  
 AAGGGGAGGGATCGAGGAGAGCTTGTAGGCAGAGAAAATACCCAAGGGC  
 AAGGGAGAAGCTGAGCCTGTTCTGAGCACACACAGTGGTTCCATCTAACTG  
 GGCCTCAGTGCCAGGTGGACTGGAGATGGGGCTGAGGAGCTGTACAGA  
 GCATTCTGGACACAGATGTACATAGTCCCTTGAGGTTAGGGTCCTTAGG  
 CATGGCAGCATTGCTTTGAGTTTTTCTTTTGTAAATGTTGCCATTCATGA  
 CAATGTGGAAGATGGGTCCCTTGACAGAGAAGGGCAGGGCTGTGAGACCAGT  
 TAGGAGACTAAGATGTGAGCCAAGGAAAATGAGGAACACCTGAACACTGG  
 GGCAGGTGCAGGGCCAGAGAGAAGCAGATGGCTTCTGAGGTTTAAAGT  
 AGGTAGAATCAAGCTGAGTGGTACAGATCTTTTATTACATATAAACTGGA  
 ATAAGCCATCTGTTCCAAGACAAAAGAGTAGGGCGGAAAACAATACAAGAC  
 AGAAATGGAATTAGAACAACCTGGGAGGAATGTGGAATTAGAGTAGAGA  
 GTCCAACACTGGCTGCAATCATAAAAATGTAAAACAACAAAAATTTGCT  
 AGGTGTGCTTACTTAGAAATAATTAGCTGTCTATTAAGTTCACTTGTGT  
 TATGGCTTAAATGTGTCCCCAAAATGTGATGTGTTGGAACTTGATCCC  
 CAATGCAACAGAGTTGAGAGATGGGACCTTTAAAAGGTGATTAGGTCATA  
 AGGGTTCTGCCCTCATAAATGAATTAATACTGTTATCATGAGAGTAGATT  
 CCTGATAAAAGGATGATCTCTGCCTCCTCCCCACAGCCCTCTTGTGCATG  
 CTTTCTGCTTTTCCACCTTCTGCTATGGGATGACACAGCAAGAAGGCCC  
 TCACCAAATGCAGCTCCTTGATCTTGGACTTTCCAGCCTCCAAAACCTGTA  
 AGCCAAACAAATTTCTGTTTATTATAAATTACCCAGTCTCAGGTATTCTG  
 TTCTAGAAACACAAAATGGACTAAGATCATTAAATTATCATTTTTTATCA  
 GACTGTTGA

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AAAATATAACAGAGAGTAAGAGGAAAATTACCTTCTTTCTTTTCTTTTCTTTT  
 CCTGCCTGACCTTATTACCTCCCATCCAGAGCATCCATTTATTCCATT  
 GATCTTTACTGACATCTATTATCTGACCTACACAATACTAGACATTAGGA  
 CAATGTGGCCTGCCCTCCAAGAACTCAAATAAGCCAAGTGAATCAGAGA  
 GGATTAATCACCTGCCAATGGGCACAAAGCAACAAGCTGGGAGCCAAGTC  
 CCAAAATGGGGCTGCTGCTTCCAGTTCCCTCTCTCTGCAATTGATGTCA  
 GCATTATCTCTCTCCAGTCCCTGTCTCCACTACCACTTTCCCCCTCAAA

FIG. 3 (16 of 52)

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CACACACACACAACAGCCTTAGATGTTTTCTCCACTGATAAGTAGGTG  
ACTCAATTTGTAAGTATATAATCCAAGACCTTCTATTCCCAAGTAGAATT  
TATGTGCCTGCCTGTGCTTTTCTACCTGGATCAAGTGATGTCTACAGAGT  
AGGGCAGTAGCTTCATTGAACTCATTCAACAAGCATTATTCACTGAG  
AGCCTTGTATTTTTCAGGCATAGTGCCAACAGCAGTGTGGACAGTGGTGC  
ATCAAAGCCTCTAGTCTCATAGAAGCTTAGTCTTCTGGAGGATATGGAAAA  
CAGACAACCCAAACAACCAACAAAAGAGCAAGATGCTGCAAAAAAAAAA  
AAATGAATAGGGTGTCTAAGATAGAGAAAAGTGGGAGAGTGCTATTTAGAC  
AAAGTGGTAAAAACAAAGCCCCCTTGTGAGATGAGAGCTGCCGACAGGAGG  
GGGCGGGTCTAGGTTGTGGGTTTTTGGGTAGGACATTGAGAGGAGGGGGC  
GGGTCTGTGGTTGTGGGTTTTTGGGTAGGACATTGAGAGGAGGGGGCGGGT  
CGTGGTTGTGGGTTTTTGGGTAGGACATTGAGAGGAGGGGGCGGGTCTGTG  
GTTGTGGGTTTTTGGGACATTCAAAAGAGTCTGAATGCACCCAGGCCTAC  
AACTTCAAGATGGTAAAGGACAGCTCCAAGGATCAGAAGAAGCATGCTTG  
GAAGTGGGCATTTTGAAGGAGGAAAAATATGCAGAGACTAGTGCTTG  
CAGAGCTTGCAATTTGAGTTTCATTGAGGTACAATGAAAACCCATTAAATG  
GGTTTACACAGTGCAATGGCCTGACCTCACTTATATTTCTAAAATAGA  
AAACAGATCAGAAGGAAGGCAATAGAGAAGCAGAAAGTCCAATGAGGAGG  
TTTACAGCAGTCATGGGGTGGGTAAGGAAAAGAAGTGGAAAGAAACA  
GACAGAATTGGGTTATATTTTGGAGATAGAACCAACAGAAGGAAGAGGAG  
AAACAACATTTACTGAGAAGGGAAAAAGTAGGAGAGGAATAGGTTTGGGA  
AATAAATCCTGCTGACATTGGAAACCCCAAGGAAGCCTCAAAAGTATATT  
TACTTGCTTTAGATTTAAAGAAATAGGAAAGAAGCATCTCAACTTGAAT  
TTGAAATCTATTTTCCATAAAAGTATTGTTAAATTCTACTCATACTCAC  
AAGAAAAGTACATTCTAAAGAGTATATTGAAAGAGTTTACTGATATACTT  
AGGAATTTTGTGTGTATGTGTGTGTGTGTATGCGTGTGTGTGTGTTAAC  
CTTCAATTGTTGACTTAAATACTGAGATAAATGTCTAAATGCTAAAT  
TGATTTCCCAAAGGTATGATTTGTTCACTTGGAGATCAAAATGTTTAGGG  
GGCTTAGAATCACTGTAGTGCTCAGATTTGATGCAAAATGTCTTAGGCCT  
ATGTTGAAGGCAGGACAGAAACAATGTTTCCCTCCTACCTGCCTGGATAC  
AGTAAGATACTAGTGTCACTGACAATCTTCATACTAATTTAGATCTCTC  
TCCAATCACTAAGGAAATCACTCTTATTAATAGACTGGGCCACACATC  
TACTAGGCATGTAATAAATGCTTGCTGAATGAACAAATGAATGAAGAGCC  
TATAGCATCATGTTACAGCCATAGTCTTAAAGTGCTGTTTCTCATGAAGG  
CCAAATGCTAAGGGATTGAGCTTCAGTCCTTTTTCTAACATCTTGTTCTC  
TAACAGAAATCTCTTCTTTTCTCATAGGAGATGCCTGAGATACCCAAA  
CCATCAGGTTAGTGAGACCAACCTCCTCTTCTTCTGGGAAACTCACGGC  
ACTAAGAATCTATTTACATCAGTTGCCCATCCAACTTGTTTATTGCCAC  
AAAGCAAGACTACTGGGTGTGCTTGGCAGGGGGGCCACCTCTATCACTG  
ACTTTTCAAGTACTGGAAAACAGGCGTAGGTCTGGAGTCTCACTTGCTC  
ACTTGTCAGTGTGACAGTTTATGTACCATGTACATGAAGAAGCTAA  
ATCCTTTACTGTTAGTCATTTGCTGAGCATGTANTGAGCCTTGTAATTCT  
AAATGAATGTTTACACTCTTTGTAAGAGTGGAACCAACACTAACATATAA  
TGTTGTTATTTAAAGAACCCCTATATTTTGATAGTACCAATCATTTTA  
ATTATTATTCTTCATAACAATTTTAGGAGGACAGAGCTACTGACTATGG  
CTACCAAAAAGACTCTACCCATATTACAGATGGGCAAAATTAAGGCATAAG  
AAAACCTAAGAAATATGCACAATAGCAGTTGAAACAAGAAGCCACAGACCT  
AGGATTTTATGATTTTCACTTGTGCTTCTACTTTTAAGTTGCT  
GATGAACCTCTAATCAAATAGCATAAGTTTCTGGACCTCAGTTTTATCA  
TTTTCAAAATGGAGGGAATAATACCTAAGCCTTCTGCGCAACAGTTTT  
TTATGCTAATCAGGGAGGTCAATTTGGTAAAATACTTCTTGAAGCCGAGC  
CTCAAGATGAAGGCAAAGCACGAAATGTTATTTTTTAATTATTATTATA  
TATGTATTTATAAATATATTTAAGATAATTATAATACTATATTTATGG  
GAACCCCTTCTCTGAGTGTGACCAGGCATCCTCCACAATAGCAGAC  
AGTGTCTTCTGGGATAAGTAAGTTTGATTTTCAATTAACAGGGCATTG  
GTCCAAGTTGTGCTTATCCCATAGCCAGGAACTCTGCATTCTAGTACTT  
GGGAGACCTGTAATCATATAAATGTACATTAATTACCTTGAGCCAGT  
AATTGGTCCGATCTTTGACTCTTTGCCATTAACTTACCTGGGCATTCT  
TGTTTCATTCAATTCACCTGCAATCAAGTCTTACAAGCTAAAATTAGAT  
GAACTCAACTTTGACAACCATGAGACCACTGTTATCAAACTTTCTTTTC

FIG. 3 (17 f 52)

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TGGAATGTAATCAATG1 . FCTTCTAGGTTCTAAAAATTGTGATCAGACLA  
TAATGTTACATTATTATCAACAATAGTGATTGATAGAGTGTTATCAGTCA  
TAACTAAATAAAGCTTGCAACAAAATTCTCTGACACATAGTTATTCAATTG  
CCTTAATCATTATTTTACTGCGATGTAATTAGGGACAAATGGTAAATGTT  
TACATAAATAATGTTATTTAGTGTTACTTTATAAAATCAAACCAAGATTT  
TATATTTTTTCTCCTCTTTGTTAGCTGCCAGTATGCATAAATGGCATT  
AGAATGATAATATTTCCGGGTTCACTTAAAGCTCACATTACACATACACA  
AAACATGTGTTCCTATCTTTATACAACTCACACATACAGAGCTACATTA  
AAAACAATAATAGGCCAGGCACGGTGGCTCAGACCTGTAATCCCAGCAC  
TTTGGGAGGCCAAGGTGGGAAGATCACTTGAGGTGAGGAGTTCAAGACCA  
GCCTAGGCAACATAGTGAGATCTCATCTCTACAAAAAATGAAAAAT  
TAAAAAATGAGCTGGACATGGTAGTACACACCTGTAGTCCCAGCTACTCG  
GGAGGCTTGAGGTGGGAGGATCACTTGAGCCTGGGAGATGGAGGCTGCAG  
TGAGCCATAATCACACCATTGCACCCCAACCTGGGCAACAGAGTGAGACC  
CAGTCTCAAAAGATAAAATTTTAAAAATGTTAAAAATATATAAAAGAGA  
ATTTTAAAAAGAACAATAATAGATCAAAGCATGGATGCAAGATATATTTA  
GTTGGAATAAAGGTTAAAAATCAAGGGATCTTGGAATTAGGTGTGGTAG  
ATTTGGGTAAGGAGTAGTCTAAGATGACCTGTTTCTTGGTACTGGAGAC  
TGGATGAGTGGCAGCGTCTTAACCATATTTTTGGTAGAAATATGGAGGTC  
TTCTCCATTCCAGGATGAATGATGAGTAAAATTTAGGCATGTAATTTGA  
GCTACTAGAAGGCACTCAATTGCAGATGTACAATGGGGAGATGATAACC  
TATCTGGAACCTCAGAAAAATACTGTATATAGATATGAAAGACATCAGTA  
GGTATGTAGTAGATAAAATCCTAAAAGTGATGTCAAAGGGAGAAGAGAAG  
TATATGGTGAACACTGTTGTTTGTCCATGCAATTGCCATCTCTTCTCTT  
CCTTACTGACAGAACCCTGATTTCACTGAGAAGTCAACATGCCCTTCCCC  
AATTGATGAATCCAATTGGTTGAAGATTATGTTCAATTCTATTCTTACATG  
ACTAAGTCACGTTGACTTAATCCTATCAAATGAGATGTCGATCTGGAAAC  
AACTTCTGGAAAAGATTTTCTACCTTGATAAAATAAAGAGCCATATAGAT  
GGTCCTTTATCTTCTTCTTCTTCTTGAATGAGATATGTTCTATGAGGAAGT  
GAAGCTTTAGAATGTGGTCAGCAACTTGCAACGACTGGGAAGTCAGAGCC  
ACACAATGAAGAATGCAGAGTGGAAGGAGAAAAAGAGCCAGCATCTCTGA  
CAACATTGTTACACCGAGAACCTACCTCCAGATTTTAAGAAAACAAGAAA  
TGCTACTGTTATTAAGCCATTTCACTGGGTTTGCTATGACTTGCAGTCAA  
ATCTAGCTTAACTGATACAGAGCACCAAGAGAACTGGTCTCTCATTTGT  
CTCATCTGTTCTTTCTAGCAGCCACGACTTTCCTAGGGTTTCTTAGCC  
CAAGTCTGGCTAGAGCAAGACTAAGTAAGACTTGATTCCTTAATGTCTT  
TTGTTTTAAGAAATATTAAAGAATTATTTTATATTAATATATTTTAAGA  
AATAAGGAAATACAAAACACTGAGCAAGCAACACAATTCAGAAATCTT  
AAAAAGTATAATAGCTGCTCAGTCTCTGATTAACAGTGAAATATGGAATC  
ATTGTAGAAATGGCCTTGGAGCGTTATTCTCCAGGCCAGCTATCCTTAT  
GGTCTGCCCCACCTCCCTCATTGCCTAAACAGTAAGAGAGTCCCATGGTG  
AGACTCAACAGTCTTAGCACAGAACTTGTTACAGTCTATTTCTTTCTTA  
CAGTCTTATATATCAATTCCAAATCAATGAGAGTAAAGCCCAATCCCTGC  
CTTTAAACCCAAAGGACAGAAGCCCAAGCCCAAGATATTCCTAACCT  
TCTCCCCCT

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CCTGTGCTCCCTATGTTTAAAGCTGGGGATCTCTTTTTCTGTGTCTAA  
TTATTTTCTCATTTGGCTTGAAAAATCTGATAAAACATTTTAGGACTGTG  
TATAAAATAGAATTAGCCAAGTGCAATGTCTTTATTCAGAAGAAATTTCA  
TGGACGTTGTGCTACTCTCTTGGCTTCTGGCTTCATGGCTTTCCAGAT  
CCACAGTAAGCTCTGGATAGTAGAAGTTATAGTAAGACTGACTTCTAAA  
TAAATGAAGTGACTTTAACCTTACTGATATGGCTTAAAGAAAAGGAGTGG  
CCTTTAAGATCCATGAACCTTCTCAAACAAAAGTGATAACGTTATCTCCAT  
GCATATATAATACTAAATATAATGCAACTGAGAGAAGTAGGCTGTGGTAA  
GAAAGGAGACCCAAGTGCCATCTGAAGGCAGCACTTACCACTCTGCTTCA  
TCCCACCGAGGAAACAAAGCATGAGTATTGCCAGATTTTCTTCTGTTCA  
AGAAAAGCCAGAAATCCAGGTTTTTGGCGTAAATGTCTGATTTTAATGT  
TGGGAACATAATTTATATTTTGAATAACATTGTGTGGGACAAGTGAACCT  
GTATGTGGAACCTGCTTCTCCAGTGGCGACCAGTTTGGACCGTTGATAC  
TCAGCAAGTTCAGCCAAGTGCGCCTTGTCAATTGTCAGTCATCAAGGTGAT

FIG. 3 (18 of 52)

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GTGTGATTGGTCAAACAATTAGTTTTGCTCAGCATCTCGTGTGTTTTCAA  
AGGACCTGAGGGTTCATTTGCCCATGCAGATCTTGTAGTCCTGTTTATTC  
TATTAATTTATCTTGCAAATCTATAATGTTTTATTTTAAGCAGCGAGAGC  
CGTGGCAGCCTTTGGTCTGGACCCTTTCTAATGATCATTTAGTATCAGGC  
TATGTGGGAGTTGATTGTTTTGCAATTGCCTGAAAGCCAACAGTATCACTC  
CTCCTCTAGGTGTGGCAGAGATGTGAGAGAGGGAGACTGACAGTCTGTGG  
GCTGTGATGCAGTGTGGGGGAAGCGAGGCACAGGGGACAATACTGTGGT  
GTATAAACTAGTCTAAGGTAGCATCAGGAAGTTCATGAAGCCAAAATGA  
TTTTCAACAGCACAAGACATTATTTGTTTTTGCTCCCTCTCATTTTTT  
TTTTTTTTTTGAGACAGAGTCTTGCTCTGTCTCATCCATGCTCGTGTGCAGT  
GGTGCATCTCGGCTCACTGCAACCTCCACCTCCAGGGTTCAAGCAATTC  
TCATGCCTCAGCCTCCTGAGTAGCTGATTACAGGTCTGCACCACCCCGCC  
GGCTAGTTTTTGTATTTTTAGTAGAGATGGGGTTTTGTAATGTTGGCCAG  
GCTGCCCTGTCATTTTTTTTTACTAGTGTCCAGTGGAGTTTTTTAGGGG  
CTACATAACATGATACTGTCTAATCTAATGGCTAATGAAAGGGATATG  
TATATGTTTTTGTGTTTAAACAAACTTCTTTGGGGTCTCAATAATTTT  
TAAGAGTATAAAGGGTCTGAGATCAAAGAGTTTGAGTCTGCTGGACT  
GGGACAGTGGTGTCAACCCAGATTGTACATTAGGGTCACTCTGGGAAGCT  
TTAAATAGTACTGATGCCCAACCTTACCGCAAACCAATTAAGCCAGAAT  
CTCTGTGGATGAGAAGTCTTCATTGTCTATCATCACCATGACCATCATCAT  
TGTCACCGTCACTACACCATTATCATCATCATCATATCATCTTCATTATC  
ATTGTTAGTATCTCCATCACCATCATCAGCATCACCATTATTATCATCAT  
CATCATCCCCACCATCATCCTCATCGGAACCTCACCTGCATGGAGGACAA  
TCCACTATGCATTAGGTGCTATGCTATTTGCTATACTCCTTATTCTACA  
ACTGCCAGAGAGGCTGATATTATCTCACTTTATAACAGGAGGAATCTGG  
ATCGGAAAAGTTAAGGTAAGCTAATTACAGAGCGAGAAGAGATAGAGCC  
AGGATTCGAAACCAGTCTCTGCTACATCAATGTTCCAGTCTTGCAGT  
ATTGAGAACCTCTTTAGTTATGCTTTCAACCCCTCCAACACCACAGTAAAT  
TTTTTCTTTTTTAAAAAAATTATACTTTAAGTTATAGGGTATATGTGCA  
TAATGTGCAGGTTTGTACATATGTATACATGTGCCATGTTGGTGTGCTG  
CACTCATTAACCTCGTCATTTACATTAGGTATATCTTCTAATGCTATCCCT  
CCCCGCTCTCCCCACCCCATGACAGGCCCTGGTGTGTGATGTTCCCCACC  
CTGTGTCCAAGTGTCTCATTGTTTCAGTTCACCTATGAGTGAGAACAT  
GTGGTGTGTTGTTTTCTGTCTTGTGATAGTTTGCTCAGAATGATGGTTT  
CCAGCTTCATCCAGTCCCTACAAAGGATATGAACTCATCCTTTTTTATG  
GCTGCATAGTATTCATGGTGTATGTGTGCCACATTTCTTAATCCAGTC  
TATCATTCGCTGGACATTTGGGTGGTTCCAAGTCTTTGCTATTGTGAATA  
GTGCCACAGTGAACATTATGTGCATGTGTCTTTATAGCAGCATGATTTA  
TAATCTTTTGGGTATATACCCAGTAATGGGATGGCTGGGTCAAATGGTAT  
TTCTAGTTCTAGATCCTTGAGGAATTGCCACACTGTCTACCACAAATGGTT  
GAATTAGTTTATAGCCCCACCAACAGTGTAAGCAATTCCTATTTCTCCA  
CATCCTCTCCAGCACCTGTTGTTTCGTGACTTTTATGTGATTGCCATTCT  
AACTGGCACCACAGTAAATTTTATAGATTTTATAAGCAAATTTGTATTTA  
CTGTGCAAGAATTGGTTTATTTTTTAAACCATGTGTTGCAACATACAAT  
GGTTAATTGTGATATTTGCTCAGTACAAGATCATCAGATCACTACACAGA  
CTTGAGGTAATTCACCTAAAAGCAAAGAGAACTGACCCCACTTAACCTG  
AGAAGTCTTTACTTATTTATTCCTATAAACGAGCCAATATGAAGAGAAG  
GCCTTAATGTGGTTAACTATGTAATTTTTTTCTGACTTTTGAATACTG  
AGAAGAGCTCATGACTCTCCCATCTCCTAATTCTACCTTGGTGGATTTTA  
GACTGACCACAACCTCATGGGTAAATGAGGGAAGACGAATAAGAAACCTTG  
CTTTTTTTTCTCCTTGTTTTTGGCTGGCTGCAGTGGCTCACACCTGTAA  
TCTCATCACTTTGGGAGGCCAAGGTGGGAAGATCACTTGAGCTCAGGATT  
TCAAAAACCTGGCTGGGCAACATAGTGAGACCCCATCTAAAAA  
AAAAAAAAAAGGCGACAGGCGGTGCGTGTAACTCTACCTACTC  
AAGAAGCCGAGGTGGAAAGATCACTTGAGCATGGGAGGTCAAAGCTGCAG  
TGAACCTTGATTGCACCACTTCATTCCAGCCTGGGTGACAAAGCAGGACG  
CTGCCTCAAGAAAACAAAAACAAACCTTAATTTTTTGGCTATTCTTTTC  
TGGTAAGAATGGTATAGAGATGGGGATGAGGATGGCTATTGTATGAGAGA  
GCAAACAGGGTCCAAGCAGTGCTCTGGGCTGTCTAAGGACCAGTAGTCAG  
CTTAACCTCTCAAATTTCCAGGGAAGGAGTTCGGAGTGGTAGAATATCCT

FIG. 3 (19 of 52)

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GGGTATGCCCAAAGCATLACCTTGCAAATAGCCTGTGATGAATAATTTG  
TTCATTTGTTATGACTGGAACTGGCTTTGTGTATGCCAGAGAATGGGG  
CAGGAAAGAGAGATTGGTGTCTTGAGCTCTCTGTGCCTCTGGGGCAGTGA  
TGCTTTTCTCTCATGTGGAAGGAGAGCATGACTGAAAAGGTGCACAAAT  
AAGGTGTCTGTGAGAGAAATTAACCTTCCAGATACAGAGACACAACCTTC  
CCCAAGAGGTCTCATTTGCTCTGCCTTTTTTCTTTTTTTTGTGTTCT  
AQCATTAAATACAGAACTGATTATGACCTCAAAAGAGAGGAGAAAGCGA  
CTCTCCCCACCCTAGAGCTAGTTAACACCATATCTTCTAGATATCCTT  
GAGAGCAATGTAACCC  
>Contig29  
GTGAACCTCGTTTTACCTGTGTAGCAGACCAAGCCGCAGACAAAATCCNTC  
AGACACCAAATTAAGAAGGAAGGGCTTTATTGGGCCTGGAGCTGCGGCA  
AGACTCACGTCTCCAACAACCGAGCTCCCCGAGTGTGCAATTCCTGTCCC  
TTTTAAGGGCTCACAACCTCTAAGGCGGTCCACATGAGAGAGTCGTGATAG  
ATTGAGCAAGCAGGGGTATGTGACTGGGGGCTGCATGCACCTGTAGTTA  
GAATGGAACAGAATGACAGGGATCTTCACAGTGCTTTTCTTATGCAA  
TAACCGATTAGATCAGGGGTCGATCTTTACCAGGCCAGGGTGTGTCACC  
GGCTGTCTGCTTGTGGATTTTCATTTCTGCCTTTTAGTTATTACTTCTTT  
CTTTGGAGGCAGAAATTGGGCATAAGACAATATGAGGGGTGGTCTCCTCT  
CTTACCTGCGGGGAGTGAGCTCAAACCTCCTTAAAGGAGTTACCTGCCTTC  
CATCATCAGGGAAGCAGGAAATCTTGCTTCTTGTGGAAGCAAGTAAA  
ACTCAAACAACAAAGAAAAAACAGGGAGTTGTACAGCAAAATAAAT  
TTTGATTTTGACCAAATTTGGGAGATCAGGAATCTCTGAAGGAGATGC  
TTTCAGACCTCAGCAAATTTGCTGTTGGTTGAGCCATAAAGTTAGCTC  
ATGCTGGTACCAAACACAGTAGGAGATTGTCAAAGGTAAGAGGCATCT  
CCACTCAGAATCCCTTCGTGGTTACCAACATGTGAACCTTGGAATCTGA  
GACAGGTCTCAGTTAATTTAGAAAGTTTATTTTGGCACGGTTGAGGACAC  
CCACCCATGACAGAGCATCAGGAGGTCTTGACCACATGTGCTCAGGGTGG  
TCTGAGCACAGCTTGGTTTTACACATTTTAGGGAGACATGAGACATCAGT  
GAATATATGTAAGATGTACTGGTTCCCTCCAGAAAGGCAGAACAACTT  
GAAGCAGGGAGGGAGCTTCCAGGTCACAGGTAGGTGAGAGACAAACAATT  
GCATTTCTTCTGAGTGTCTGATTAGCCTTTCCAAAGGAGGCAATCAGATAT  
GCATTTATCAGTGAGCAGAGGGGTGACTTTGAATAGAATGGGAGGCAG  
GTTTGGCCCTAAGCAGTTCCAGCTTGACTTTTCCCTTTAGCTTAGTGATT  
TGGAGGCCCAAGATTTATTTCTCTTCTACATCACTGTGGGCAGCTGACT  
AGGAAAGCTTTGTAGGACTGGTGGGCAGTGTGAGAGCCAGTGGGGGGTG  
GTGGTCTCTGTGCCAATGGTAGCAACCACCTGTGAGGCTGAGTAACTCAT  
TTCCCAACCTCTCTAGCAGCCCCAGTGGAGATACAGAGGAAGCAGACTA  
GCGATACAACCCAGCCTGAAGTTTTGTCTGGTGAGTGAATGGAATAAAA  
ATGGGAAGGGTGCTGAAGAGACCAGCAAGAAAATGGTTGAAGAGATGGGG  
CACAGAAATTAAGCTGGATCAAAAAGGACGGAAAAGCAGAAAGGGCCGAT  
AGAGAGAGGGGATATCTATGGGTTGCGGATTCTGAAAAGGACAAATCACT  
GGTGCTTTGAGAAGAGAGAGGGGTGAGAAAGCAGGAAGGCTGGAGGCTGTC  
ATCCAAGAGGCGGACATCTGTGAACATGATTCCAAGAGTCACCAGACCAT  
GGGGGTGCCAAAGGGAGTGCCTCTTCTCACTCTCTACTCTTAATTCCTT  
GTACTCAAGATAATAAGTTCCAGAAAGAGAAGTACCCATATTTAATTCAT  
CTGTGTCTTCTAGCAGTACTAAAAATATTATATGAAAGGTATCAAACCT  
TTGAGAAATGTGTGCTGCTAAATTTGTTAAGGATGCTGGAAAACCTCAAGACG  
TCCCTGATCCTGAGCCTGAGTATGAGCCTGTGGTGAGCCCAATGCAGGTC  
TCCATTGAGACAAAGGCCTCAGGGAACGGATGAGACCTAGGGACAGAGAT  
GCATGCTGGAGCAGCATTTCCCATCTCTACTGCAGCTCAGGCCAGCTGAC  
TGCTTTATGAGTAAACGTTACAGGGAACACTTTGCAGTCTTAACACACA  
TGCCCCACCTGTGACCCTGATCCCTGTTGGGTGACCACTGACATCAGAGA  
TTTCGATGGCAGCAATGAAGACAAGGCTATCCTCATTAGGAAGGAAAGGAA  
GGAGGAGGGAGGAGGGCAAACGAATCTTTCTGCTTGTCAACCACGTCCA  
TCTCTGTTAGGTGATTTCCCATGTGTGACTTTGTTTATCTTTATAATAAC  
TCTGAGAGGTAGGTCTTGATGTCCACATTTGAACATGAGGACATCCAGC  
CAGGAAGTTGAGTTCTGGGACATAGCTGAGAGGGCAAAGCTACATATAA  
ACCCCTCTTTGTTTTTCTGGCTTATCCACTGAGTGCCCCCTGCAATCCA  
CCAGCCCATTTGTGAAGTGCATACTATAGGTAAGTTGGCACAGGAGGAGT

FIG. 3 (20 of 52)

GGATGTGGGCGATTTTGACAGCTCTCCAGGAACTTACACACTGGTGAAG  
GAGGGCCAGGTATGTTCCCTGACCAGTCACAATCAAAGCAACCTCCTACTA  
ATCAGGGAGGCTTGGTACCTGGGGAATGCTATGTTGAAAGGTTCTTTTCT  
GGGTTTTAAATGATGGGTCTATTTCTTATTCTTAAGATTGCTTTTTTT  
CTGGCTAGAACTTAAAGAAATTTTCAGTAAATTTCCCTTCCCTGGCAC  
AAAGTGAGCTTGAATGAATTTCCAGGTGGCCTTGATACTTTAAATATT  
GCCTCCTATAAAATCAACCTTTAGAAGAAGGAAGTCAAAGAACATGCTAG  
ATTTACAAAGGTTAATTCCTTGAAATCCAGTTATCTACAGGACAATGTT  
GTCAAAGAAAAATTTTGGCCAGGCACGGCGGCTCATGCCTATAATCC  
CAGCACTTTGGGAGGCTGAGGCAGGTGATCACCTGAGGTGAGGAGTTCGA  
GACCAGCCTGGCCAACATGGTGAAACCCCATCTCTACTAAAAATACAAAA  
AAAATTAGCCAGGTGTGGTGGTGCCACCTGTAATCCAGCTACACGGGA  
GGCTGAGGCAGGAGAATCGCTTGAACCCGGGAGGAGGAAGTTGCAGTGAG  
CCAAGTTCAAGCCACTGCACCCAGCCTGGGCAACAGAGCAAGACTTTGT  
CTCCAAAAAATAAATCAATGATATTTTAAATTTCATGGTAAGGAA  
GATTTTATTTCAGAACCCAGCACAGAAGATATAGGAAACACTGCAATGGGAC  
TTTGCGGTGGGGGAGAGAGATTGAACACAACACTACATATACAGCACGGGCA  
AGGACATATTTCATGCCAGGAAGCAGAGCAAAGATCAGTGGATGCGAAAT  
TACTAAGAGGAAACATGAAAAATAAGGGAGCTTCTGCCATAAACCCACCTA  
ACCGGATCCTTGCTGAAGACAGGACAGGGTGATTGGACACCACTTTGGGG  
ATGGTGGAGGATGGGGAATCCAGTGAGATTTCAAGGGTGATGCGATATTG  
AACATACAAAGTTCTTGCTAAAAAAGGATTTTACAAGAAAGTGACAAAT  
GTGCTGGGACAAGGTGCAGGAGCCCCGACGGAGATGTGGTCCAGCAGAGA  
ATATGTGCCGAGATGATAGGTGAGTTCTCTGACGAAGGATATATGCTGAT  
CCAGCCAGGGTGAAATGCTCAGAGAAAGCACGGAGGGGCTATGTCCGTTG  
CCCCAGTCTCCACGCGGTCAAATCTGATCCCGTTGTGAGTGTGGCCGTTT  
GTAGAAAGCAATCAGGGGGGGTCCCTCCCC

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AATATATATTTTTATANNATNTGAGACAGGTTCTCACTAGGTTGCCAG  
GCTGGTCTTGAATTCCTGCCTTCAAGTGACTCTCCACCTTAGCCTACTG  
CATAGCTGGGATTACAGGCACAAACCACTGCATGCAGCTAACTTTGCTTC  
TCATTCCAGCACTTTTATTCCTGATTATATGTATATGTATATCTGCA  
TCATCTCTCTCTCTCTCTCTCTCTCTCTCTCTATATATATATATATAT  
ATGGAAATATCTCTCTCTCTCTCTCTATATATATATATGGAAATATATATCT  
CAGTCTCTCCTATCCTCCTTTAATCAGTTTTGCTATCCTGTCAATTCCCC  
CAACGAGTGTGATGTTGTGAAATATATATTTGTTCTTCATCTCCTGTTTC  
CTGACATACAGCTTTTAAAAACCCCTTGAATCTCTGGAATAATAAGAGTG  
TCTTTTGCATGCTAATAGATGACTGCTGGCTGGCAGCCCCAATGCAGTAG  
CTTCATGATGGGTTTGTACAGGAAAGACCAAGGCAGGATTGGAGACTT  
GAGACTGTTAGCCCCACTCCCCAACCCTGGAGGGAGTGGAGGGGCTGAA  
GGTTGTGTGAGTCACCAATGGCCAATGGTTCCGTCAATCATGTGTATGTA  
ATAAAGCCACTCTTAAAAACCCAAAAAGGACAGGGTTTGAAGGGCTCCC  
AGATAGCTGGACACATGAAGGTTCCCTGGAGGGTGGTGGCCAGAGGGGCA  
TGGAAGCTCCACACCCCTTCTCACATGCTTTGCTCTGCGCATCTCTTCAT  
CTGGTGTTCATCTGTATCCTTTGTAATATCTTTAGAATAAACTGGTAAA  
CTTAAGTGTTTCTCTGAGTTCTGTGAGCTGCTCTAGCAAATTCACGGAAC  
CCGAGGGGAAGCAAACCCAGATTTATAGCCATCAGTCAGAAGCATAGGTGA  
CAACCTACCCTTGTAACTGGCACCTGAAGTGGGAGGCAGTCTTGTGAGA  
CTGAGCCCTCAACCTGTGGGATCTAACGCTAACTCCAGGTAGATAGTGTT  
GGAGTGAATTAGGACACCCAACTGGTGTGCGCTGCTGGAGGACTAGTGGT  
GGGAGAAATCCCCAAGCATTTCGGTGACTAGAGGTACAGAAGAAGTCTAG  
TGTTGAGGTGTTGTGACAGTATGGTAGGGAAACTGCGTCTGGTTTTTTC  
CTTTACAATCAGTTAAATATTTAACACAAGTCTACTGTATATTAGTAAA  
AGGGTTACATTTTTTAATGTCTTGACAGTTGCACTTTGACAACCTCCATA  
TCAATCACTTTTTTTCGTGTCCGTTTGAACCAAAATCACTTGGGATACC  
ATGAACCAGGCTGCAGCGTATTTCCAGGCCTTGAAAGCTTGGAGGCCAT  
TTTGCCAGCCNTAATCCCTGTGAATACCAGGCTTCGTGGATTAAAAAAT  
AGACTTGAGGCCAGGCCTGGTGGCTCACACCTGTAAGCCAGCACTTTGG  
GAGGCAGAGGCGGATAGATCAAGGTTAGGAGTTCGAGACCAGCGTGCC  
CAACATGGTGAAACCCCGTCTCTACTAAATATACAAAAAATAAGCCG

GGCGTGATGTTACAGC LAGTAGTGCCAGATACTCAGGAGGCTGAGGLAG  
GAGAAATACTTGAACCTGGGAGGCAGAGGTTGAAATGAGTCAAGATCGTG  
CCACTGCACTCCAGCTTGGGCGACAGAGTGAGACTCAGTTTTAGGGGAG  
TTAAACAATACAAAAAAGAAAAAGACTTGAACAATGAGGCTCCACTGG  
ATGGATTTAGGGGAATTACAGGAAGCAGGACCTGACGGTGCAATGCCACA  
CTCCACCTGTCCAGAATTGGACCTCACCAAGGGAGGTCTGTGGGACAGG  
GAGAGGCCCTCTGCCTCCACCCCTCCTCTACTCCCCAAACCTGAGTCA  
GGCTGAATGTAGTAAACCTGGAACAGAAAAGTTCAGTTTGGCAATAGGTA  
TCTGAAGGACTCCAGGTGCTTCTCCCTTGATTCAAAATTTTACTTATAAA  
AAAAATTATAAGAAAATTCTACTTAAAAGAAATAATCAGGGAGGTACAAC  
AAATTGTACTTTTTTTTTTTTTTTTTTTTTTGAATGGAGTCTCACTG  
TTGCCCATGCTGGAGTACAGTAGTGTGATCTCGGCTCACTGCAACCTCCG  
CCTCCTAGGTTCAAGTGATTTTCTACTTCAGCCTCCCAAGTAGCTGCGA  
TTACAGGTGTGTGCCACCACACCCGGCTAATTTTGTATTTTGGTAGAG  
ACGGGGTTTACCATTGTTAACCAAGATGGTCTCGAACTCCTGACCTCAGG  
TGACCCACCTGCCTCAGACTCCCCAAGTGTGGGATTACAGGGGTGAGCC  
ACTAAGCCAGCCATTGTACATATTTTGTGGGTATTTACTAAAACATTAT  
TCAAAATAGTAAAAAAAATTGAAATAAACTGGGACTGGTTAAATAATT  
TTGGGTACAACCATGATGGAATACTATACAGCCATTAAAAATTACATT  
GAGGCCAGGTGTGGTGGCTCATGCTTGTAATCTTAGCACTTTGGGAGGCC  
AAAGTGGGAGGATTGCTTGGACCCAGGAGCTCAAGACCAGCTTGGGCAAT  
GTGGCAAAACCCCTGTCTCTAAAAAAAATACAAAAAAATTAAAAAGCT  
GGGTGTGGAGGCACACACCTCTAGTCCAGCTACTCAAAGGGCTAAGGTG  
GGAAGATCACTTGAACCGGGGAGGTCAAGGCTGCAGTGACCCAAAATCGG  
GTCATTGCACTCCAGCCTGGGCAACAAAGCAAGACCTGTCTCAAAAAA  
AAAAAATACATTGAAGAATATCTTACGGTATGGATAAATATTCAATTTA  
CAGTGATAGATGCAATAAAAGCAAATTACAAAATATACAGTTTAATTCC  
AACTTTGATACTACATATGTATATATGAATACATGCATATGTTATGTATG  
TATATGTAAATATAACAATATATGTTCTATATATGGATATTATATATTTA  
CACATACATACACATATATAATATCTTCTCTAGAGAGCAGAAAGAGAG  
TAGACAGATAATGAAGATAGGATACAACCTCCAGTCCAGCTCAACCTAGGG  
GACTTGTTTTAAAGCCTCAGGAGAGAGAAGTTGGGACTAGAAAGCAAGGC  
AGCTATTTGTAAAGCATCTTTGTGTTTCATGCTATTGGGGTGGGAAACAAC  
AGCACAACTTTTGAAGGCCCTTTCTACTACCCCCACAACTGCAGAGCA  
GCTTTAGGACCCTCAGAGTTCAAGAAGACCATTTCAGAGTAGAAGAAGT  
AAAAACATGTATGAACCTGACCTGAGCTCATGGACTGTGCCATGAGGGA  
AATTCCTAAACAGCAGGAGAGGCCCTGGAGGAAGGCAGAGGCCCTGCAT  
CAGCAAGTCCAGGCAAAAGCCTGCATTCCATAGATGCTCATCTCTGCG  
TGGTGAGGTCTAAAGACGTTTGGTCTCAATATTAAGTCTCGTGAGAGAGG  
TCACAAACCCAGTCCCTTGGCCACAAAGGAAATAAATTCTGGCTTGAGA  
CATTAGGGAGGAACAGGGCAAGGGGAGGTTCAAGAAAGTTTAAATGGATG  
AGATGATATTTAAGCAAGGCCCTGGAAAATGAGAATTTCAACCAATAGCC  
ATATGGTAGGTGAGAAAGCAAGATAAGGAGGGGGCAAGTGCAAGGGGCA  
ACATCAGATATGACCAGGGTGTCTGTTGGGCGATGGCTGATGGAGAAGAAGA  
TTAGACTGGAGTTTGGGAATGCCACAGTATCGAGGTTGGATTTAATCCTA  
TGGGTAATAAAGCCAACTGTTCAACCCCCAACCCACTTGCAATATGGCTC  
CAAAATAGCAGGTGTTTGATAAAATGACTACTTTTACTCTACTATTCCCT  
CCCTCTTAAGAAGAAAAAGAAAGTGGAGGCTCAGAGAAAGGCAGTGGCTT  
GTCCCAATCACACTATGATTTGGCCACAAAACAAGAACGAAATGTTACAC  
CCAAAAATGCTGCCTCCACCTCCCTTCCTTGCTTTCCCTCCCTGCTGGACT  
ACAGACTATCTCAAGAGTGACGTACACCATCAGGGCTTCAGCTTTTCCCC  
GAAACAATGCCAAAATATTAGCCATACGTCACTGTAGTAAGAGCCCTGAA  
TTGGGAATCCCAGCTTTGACGCAGACATGCTGATTGACTCTGTGACCATT  
CTCTTCACTTCTCCACTCTATTCTTCCCCACCTGTAAAGTGAGGTCTTT  
CCAGTTATAAAAAACAGATGATGCTATTGTCTGTTTTGTATCTAATCTTG  
CTGTGTTATAAAAAAAAATAAGGCTCTGTACATTCTTGGCCAATTC  
CCTTCTTATCTCTACTTCCCACAGCCCCTTTTTCTACAGAAAACCAGCAT  
TGTTCTTCTGGATCCATCTCTTAAGAAAGCGCTTTGCCTCCCCGGTTATT  
TAGGTGATAAGAAAGTGTCTTAGATGACAGCCCTGGAATGGGCTGGAGGCA  
ACAAAAAAGCAAGTGAAATAGACAGTTACAGCGACGACAATAATAACAAC

FIG. 3 (22 of 52)

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CAACACCTCTCACTAAAGAGAAAGAAATAAAAAAGAAAATTAAAAATCTGC  
CGCAATGCCACACAGTCAATTGAATAACTGCATGTGTACAGCACTTGGTT  
ACTTTTACATACTTCATATTTTAGCCTTCATAGCAGCTCACAGGGGTGGA  
TTTAATTTTGTAGTCCAACCTCCTGTACGGTGCCTGGCACAAGTATAATAA  
ATGTTCTGTGAATAAATGACCCCTCTTTTAGATGAGGAAATCGAGGCTCA  
AGGAGAACAAGCAATGTAATGTCCCCCTCCTGTTGAGCCATCTGCCTTTC  
ACGCCACTGAATGCAGTAGTCTCAGTGCCTGAACTTGACCCCTCTTCTG  
CTTTTCGGACTGGTCTTCTAATCCCGTTGTGACTCACTACACCACCTCT  
CCTGCATATGACATCTACATTTTAAAAACAAACCGTATGGAAATAACACAT  
TAGTCGGCTTGTTCCTCCACCCCGCAAAAAAAGGCCTCTTTATAACA  
GAAACTCTCAGGTGGTAGGGGAATTTATTCCCCATTATGGGTAGAA  
AGGCCCTAACCTTGGACCTCACGCCATAGCTATTCACATGGGGGAATGAT  
GAATAACATGGGGAGCAGCATGTAAATATCATTGAGCCGTAGTCCAGACC  
TATAACACATC

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GGGGGAGCTGCATGTGCCTGTGAGATCTGGGGGAGGAACAGGAAGATCA  
AGAGTTCTGTGTAGGACATGTTAAGTTGAAGGTGCTTACAGGATAGCCAG  
ATGAAGCATCAGGTGTGCGATCAAAGATATGAGTCTGGAGCAGCACATCC  
TAAGTCACCTCCTGCACCAACACAGAAGTTCAGGCCACTCACTTGAGCT  
CTCCCAAATAGTTTCCAAGTGTCAATTATGTTAATAACCTATGAGCTTGAA  
CACCAGATTCAAACCCCACTGCATGGCTTTAAAGACCATCTCAAGGGCT  
TGACACTCCAGGGAGCCAAGTAAAGATGCCTGGTCTTACCATCAACCTCC  
ACCCCATTTTTATAGAAAATGTTTCTACCTGTCTTAAGGCAGGGTCTG  
CCCCACTCCAGGCCCTTTAGATCCCAATATTCTCTCTCCCTGAACCA  
AAACCTTCATCTCTCCAGCATGGGTGGGGCTCCATTCTTGCTTCTGC  
TCCCTGAGCAGAAGCAAGTTTCTCCCAACTTGACCTGATTCTCCTCCTA  
AGTACCAGTCACTGCTTTGTTTCTGGAATGAGAGAAAAAGACAGAGTGAG  
AGAGACAATCCAGAACTCTTGCTCACTCACAGCTAGGCTGGGCATCTGGG  
AGGATGGCTGTGTCCATGGGAACCTGGGAAAAGCCACACCCTTGGCACCC  
TGGTCACCCACCTGTCTCCCTGGCAGATTCCGCACTGCTCTCTTGACCC  
TCTACCAGGGCTAACCGGCCTGCTCACTCTCCCCAGCATGTCTTCCACG  
CCCCTCTCATCTTATTACATTTCCCTTCACATAAACTGCCCTTCTCTCC  
AATCACCACATGTTCACTTCCCACCCAGCTGTCAAAGTCTGGCTCAACCT  
CATTCTTGAAAAGGAAAAACAAACAAACAAACAAACAAACAAAGCAAAAA  
ACCTATGATGGATTAAGAACACACTTCATTCCAGGAACATGCTTATCTCC  
TCTAACTCTCACAACAACTACAGCAGGTAGGTGTTATCACACCCATCTCT  
CAGGTGAGAAAACAGGCTCAACGAGTGCAGGAGGACACAGCAAGTCAGTG  
ACAAAGCTTAAATTCAAGCCCAAGCCTGTTGGCAACCAACGTCTGTACCC  
TTGATAGCTACCTCATTACCCACCAATCCAGTGGCCTCAGGCCTGGCTG  
CACACTGGGATCACCTGGTGCCAGACCACATCTTAGACCAGTCATACAG  
AATCTCTTGGGCTGGGATCCTCCACGGTACATTTTAAGGGTCCCAGGTG  
AGTTCCACCATGGACCCAGAATTGAGGACCCAATACCGTATACCATCTCC  
TTCTTCATCTCTTCTAAGGCATCTCTTACTCGCTGTGCACTCCCATACCA  
CTTTGTTCAATCATCCAATCATTCAATTCATTGAGTCAGTTAGTCAGGAGC  
TACTCACTAGTCCCCTGCCAGGTCTTAGTCATGACATAGGGCTCTGGGA  
CCAACAAGAAGCAGGACCCATGCCTCCTGCTCTCATGGAGCTTGCTCTGC  
AGCAGAGGAAGCAGTCAGTGAGATGTAGCAAATGTGAAATGTGCACAGAT  
GGGAAAAGCAAACTTTAAAACTTTTAGGACAAAATACACAAGAAATCTT  
TGCAACTTTGGGACAGGAAGGAACAACATTCTTACACATGACACCAAAG  
GAATCAACCATAAAATAAAAAGGTGATCAATTTGACCTCATTTAAGTGTTA  
AGCTTTTTTTCATTGAGAGACACCATTAAAAATTAAAAATACATGCCACAA  
ACTGGGATACAATTTACAACACTTATGTCTCACAAGGATTAGTTTTC  
AGAATATATAAAGAACTCCCGCCGGGTATGGCCGCGCACGCTGGAATCT  
CAGCACTTTGGGAGGCCAGCGGATCACATGAGGTGAGGAGTTCAAGACCA  
GCCTGGCCAACATGGCAAACTCCGTCTCTACTAAAAATACAAAAATTAG  
CCAGGCATGGTGGCGGGCGCTGTAAATCCAGCTACTCAGGAACTGAGG  
CAGGAGAATCACTTGAGCCCAGAAAAAGAAAGTTGAGTGAGCTGAGCTC  
ACATCACTGTAAGCCTCGGTGACAGAGTAAGACTGTCAAAAAACGAAAA  
CAAAAAACAAAACTCTACAAATAAATAAGAAAAAATAGCCCAGCAGGA  
AAAAGTATATACATTTCTAAAAAGAATAAATACATTTCTGTCAGTTTCTA

FIG. 3 (23 of 52)

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ACATATATTTTTTAAGAGTAAATACAAATGGTTAGGAAACATTTTTTAAA  
ATGCCCAACCTCATTAAAAATTATAGAAGTGAAAATTAAGCCACAATAAG  
ATACGATTTTATACCAAATACAGTGTCAACACTTTGCAAGTCTGACCTCA  
CCAAGTGTACCAGACGTGTGCACTGACGTGGCTGCTGAGATACTGATGG  
TGGGTCTGTAAATCTGTACTACAAACAATTGCAATAAAATGTAATAAATA  
TACAATAGGTGGAGCAGGAAGTGACCTGCAACCATATAGCAGATAGGGCA  
GGAAAAAGCCTATGAAAGCTGACATCAAAGGGATAAGTTCCAGTTACCCA  
GCTGAAGGGAAGGAGGGTGTTCAGATAGAGGAAGGATAAGCATGACCTA  
TTCAAGGCCAGTGAAAGAAGCGTGCACGGCCAAGTCAGGAGAACCTGAA  
ATTGTGTCAAAGAGCTTGGATGCAAAGAGCCGTGGGAGACTATTGGGGGT  
TTTAAGCAGGGATATAATATTCAATCAAGCATGCAGTAAAAGGTCACTGG  
CACCTGCCATGGGCCAGGACTCGGGCTCTACATGATTGCGTCTGTTTTGG  
AAATATCACCTCGCTGTGAGATGAAGAACAGGTAGGAGGGTCACAAAAC  
TTGAAGCAGAGAGACTGTTGAGGAAGTAAGCTGTTTTTGTGTGGACTGTG  
GCAATCACAGAGGCAGAGGATATAAATGCACAGAGACACAAGGCATGTGG  
GAGGCAGAAGGAATCAAATACAATGAGTGATCAGATGTGGGGTAGAGTG  
GTGAGTGAGAGACATACTCAAGGTGACACGCCAGGTATCTGGGTGGAT  
GGTAAGACATTCACTGGACTAGGATCGAGGAANGAGGTGGGGAATGGGACC  
ATACCTGCAGTTTATAAGGGGTGGACGAGGGAAGATTATGCGGGAGACTG  
AGAGAGGAATAGACAAAGGAATCCCGGTGCAGTATTACAGAACTGGGGT  
GGGAGGGGGTGTANTTCAAAAAGGAAAGAAAATTGTCAAATAGTATGAA  
ATGCTGCAGAGAACTCACGGATTTTTTTTTTAAGCTTAGAATTATTCAT  
TGACTATGTGAATAAGAATAACTTTTATGAAAGAAGTTTGCTTAAGTAG  
TAGGAAGAAGCAAAATTGTTGAGGGCTGATGAGTGGGAGGAGAAGTAATT  
GAAGGCACCTTTTCAAGAGAAAACAAGCAGAAGGTGAGGAGAATACTAAT  
GAAGGAGTTACGGCCTTCACTATTTTGTGTTTTGCTTTAGATAAGCAAGACT  
TGAGTGGGTCTGGTGAGGAGAAAACAAGTAGAGTACAAAGTTAAAGGAGAG  
ACAGACAGAGATAGAGATAGGGACAGAGAGAGAGACAGAGACAGAGCACA  
AAAGAGCAAGGTCCCTGAGAACACGGGCCTTCTGTTTAAACCCAGCCAG  
ATGTATTGCAATTCAATCCAGTACTAACCAACCAGAGTTTGTGTAGACT  
CTACAAGTTAAAGATCTGGTCCCCAACAAAGACTGCTTCTACGTCAGATG  
CCAGGCACACTTCAGGGGTCCCCAAGCCACTCATGTTTTTTGAATGACTG  
CCATAAGTTCAAAAATTCCCACAATTCTCTCAGATTCAATAACTGGGTAT  
AACCCTCATAGAATCAAGAAAATGCTATCATTATTATTACAATTTTAT  
TATAAAGGATACAAATCAGAAGGACTAGCCAAATGAGGAGACACATAGAG  
AGAGGACTAGTAAAAAACAGAGCTTCTGCGTCCCTACCTTCAAGGAATCAG  
GATGCACCACCCTCCAGCACATCAAGTGCTCATCAACCAGGAAGTTCCT  
CTGAGTCCCAATGTCCAGAGATTTTAGGGAGGATTCATTACATAGGTATC  
ATTGATTAAATCATTGGCCATGTACTTGAAGTCAATCTCCAGTGTCCCTC  
TTCTCCCTAGAGGTCTGAAGGGTTGGCTAATATCATGTGGCTCAAAGCCC  
CAACTCTAATTACCTTTTTTGGTCTTTTCAGGGACTAGACCCCATCCTGAA  
GCTATCTACAGGCCCTGCCATGAGTTAGCTCATTAAACATAACAAAGACAC  
TTATATTACTCAGAAAATTCCAACAGTTTTTAGAAGCTCCATGTGAGGAAC  
CTGGGACATAGATCAAATCTTTTTTTTTTTTTTTTTTGGAGACAGGGT  
CTTGCTGTGTTGGCCAGGCTAGAGTGCAAGGACAGATCACAGCTCAATGC  
AGCTTCAACTTCCCAGGCTTAAGTGACCTTTCCACCTTAACCTTCCAAGT  
ATCTGGGACCACAGAAAATGGCTAATTATCCTGGCTGATTTTTTAACTTT  
TTTTTTTTGTAGGGATGGGATCGCCCTGTGTTGCCAAGGTTGGTCTCAA  
CTCCTGGGTTCAAGCAATCATCTGCCCTGGCCTCTGTGATGGTTAATAC  
TGAGTGTCAACTTGATTGGATTGAAGGATACAAAGTATTATTTTTGGGTG  
TGTCTGTGAGGGTGTGCCAAAGGAGATTACATTTGAGTCAGTGGACTGG  
GAAAGTCCACCCTTTCCAGTGGACTGGGAGAGCCACCCTCAATCCAGGT  
AAACACAATCTAATCAGCTGCCAGTGTGGTCAAGATAAAAAGGAGGCAGAA  
GAACAGGGAAACACTAGACTGGCTTAGTCTTCCAGCCTACATCTTCTCT  
CATGCTGAATGCTTCTACCTCGAACATCAGCCTCCAAGTTCTTCAGTT  
TTTGGACTCTTGGACCTTCAACCACAGATTGAAGACTGCAGTGTGGCTT  
CCCTGTTTTTGGAGTTTGGGACTCAGACTGGCTTCTTGTCTCCTCAGCT  
TGCAGATGGCCAATTGTGGGACTTTAACTTGTGATCATGTGAGTCAATAT  
TCCTTAATAAAGTCAAGATATATATATATGATCAGACATATATATATAT  
CTATTGTATATTATATACAGATATATAATATCCTATTATATACAGATATA

FIG. 3 (24 of 52)

TAATATCCTATTATATACAGGTATATATATATATATGTATCATATATA  
TATCCTATTGGTTCTATCCCTCTTGAGAATCCTGACTAATACAGCCTCCC  
AAAATGCTGAGATTACAGGAGTGAGCCACAGCCACCATGCCAGCCCCAA  
ATTCTTAATTATACAACAATGGGTCCAGAGATCAGGGCCTGGGTAGGATG  
CAGCAATAAGAAAACAGATGGTGGATGGGGACACATGTTGGAAGTGTGGC  
AGGACATGGCTGAGGGAACATAGGATGGTGTCTATTTTCATGGCTGAG  
TGTGAGGAACAGCATAAGGTCAAAATTTGAGGTCAATGGTGAGTTTTTTA  
AATTGTTGCTGTGAACCCCAAAATCTGACCCAGGTCTCAGTTAATTTAG  
AAAGTCTATTTTTCCAAGGTTGAGAACACCCACCCACTCACGACAAGAGC  
ATCAGGAGGTCTGACCACATGTGCCAAGGTGGTAAGAGCACAGCTTGG  
TTTTATATATTTTAGGGAGACGTAAGTCATCAATCAATATATGTAAGATG  
TACACTGGTCTGCCTAGAAAGGCAGGACAACTTGAAGCAGGGAGGGGGC  
TTCCATGTACAGGTAGGTGAGAGACAAACAGTTGCATTCTTTGAGTTTC  
TGATTATCCTTTCCAAAGGAGGCAATCAGATGTGCAATTATCTCAGTGAG  
CAGAGGGATGACTTTGAATAGAAAGACAGGCAGGTTTGCCCTAAGAAGTT  
CCCAGCTTGACTTTTTCTTTAGCTTTGTGATTTGGAGGCGCCAAGATTT  
ATTTTCCTTTACATTTCCCCCCTTTCTTTTAAAGAATCTTTTAAAGAA  
AGCTTTTAAAAAGAAAATGAGTCTCTGGTCCCAGGTTTCATCTGAATTCT  
CGAGGGGAGGATGGTTTATCCTAAACGGGTGGTTCTGAATTTTGAGAAAG  
TGCATTGTAC

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AAAAGCCATACGAATGAGGAAGAATTAAGGGCCAGAACAAAACAAGAAGA  
TGAGGGAAAGTTTGAACCTTCTAGAGACTGGCTAAATGGTTGTGACCAA  
AATGCTGATAGTGATACGGACAATGAAGTCCAGGCTGACAAAGTCTCAGA  
TGGAATGGGGAATTTGTTGGGAACTGGGCAAAGGTCAACCTTGCTATGA  
CTCAGCAAAGAAATTTGGGTGCATTGTGTTTCATGTCTGGGGATCTGTGGA  
AGTTTGAATGTAAGAGTGATGACTTACGGTAGGGTATCTAGTGGAAGAAA  
CCTCTAAGCAACAAAGTGTGTTGCTTAGAAATTTCTTTCTTTCTTTTTT  
TTTTTTTTTGAGCTGGAGTTTGTGCTGTGTCGCCCAGGCTGGAGCGCAGTG  
GCGCAATCTTGGCTCACTTCAAGCTCTGTCTCCTGGGTTTCATGCCATTCT  
CCTGCCTCAGCCTCCCAAGTAGCTGGGACTACAGGCGCCTGCCACCATAC  
CTGGCTAATTTTTTAGTATTTTAGTAGAGACGAGGTTTCACCATGTTAGC  
CAAGATGGTCTCAATCTTCTGACCTCGTGATCCACCCGCCTTGGCCTCCC  
AAAATGCTGGGTTTACAAGCATGAGCCACCCGCCTGGCCTGCTTAGAAA  
TTTCTAAGCCAGGATATGGCCTGTCTGCTTCTAACAGCCTGTGCTCAGGG  
GTAAAGAAATGACTTAAAGTTGGAACCTATGTTTAAATGGAAGTAGAGT  
CTAAAAATTTGGAATTTGCAGCCTGGCCTTGTGGCAGAGAAAGAATCC  
AAGTAGGCTGCAGAGCAATCATGCTAGAGAGATTAGCATGACTAAAAGG  
GAGCCAAGTGCTAATATTCAAGACAATGTTAAAAAGGCCTTGAGGGCATT  
TCAGAGATCTTAGAAGCAGCCCCCTCCCATCACAGGTGCAGAGGTTTGGTG  
CACTAGAGCCCATAGGTTTATGGGCCANNGCCAGGGCCACACTGCTATGC  
ACAGCTTTGGGACACTGCTGCCCGCATCCAGGCCACTCTGCTCTGGCTCC  
ACCCCTTGGCTCAAACGGGCCAAGATAGAGCTTGGACCACTGCTCCCGAGG  
GCACAAGCCATAAGCCTTGGTGGTTTCCATGTGGTGTAAAGCCTGCAGGT  
GCCCAGAATGCAAGATTGAGGGAGCTTGGGCACTTCCACCTAAATTTTCAG  
AGGATGTGTGAGAAACCTAGGTTCCAGGCAGAACATGATACAGGGGC  
AGAGCCCTTGAGAGAACCTCTACTAGGGCAATGCCAAAGGAAAATGTGG  
GGTTGGAGTCTCACACATGGTCCCCACTGGGGCACTACCTGGTGATACT  
GTGGGAATGGGCTGCTGCCCTCCAGACCCAGAAATGGTAGATGCACTGG  
CAGCTGGCACCCCTGAGCCTGGAAAAGCTGCAGGCACTCAACTCCAACCCA  
TGAGATCAGCCACATGGGCTACTCCAGGGAAGCCACAGAGGCAGGGCT  
GTCTAAGGCCCTTGGGAGCCTACCCCTTGAACCAGCTTGCAGGACATGGAA  
TCAAAGATTATGTTGCAGCTTTAAGGCTTAATGTTTTCCCTGTCAATTT  
AGGCTTGTGTGGGACCTGTTGCTTTTTTTTTTTTTTTTTTTTTTTTGGT  
CAGAGGTGTTGAACCAGAACAAATTCATCTTGAATAGGGGCTGGGTAAA  
ATAAGGCTGAGACCTACTGAGCTGCATTCTAGGAGGTTAGGAATCTAA  
GTCACAGGAGGAGATAGGAGGTGGGCACAAGATACAGGTAGCGAAGACCT  
CGCTGATAAAATAAGTTGCAGTAAAGAAGCCAGCCAAAACCTCACAAAGCC  
AAAATGGTGATATGGTTTGGCTCTATGTCCCCACCCAAATCTCATCTCAA  
ATTATAATTCCTAATCCCCACATGTTGAGGGGAGGACCTGGTTGGAGG

FIG. 3 (25 of 52)

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TSATTGGATTATGGAGGCAATTTCCCCCATGCTGTTCTGGTGATACTGAG  
TSAGTTCTCATAAGATCTAATGGTTTTATAAGTGTGGAAAGTTCCTCCT  
ACACACATGCTCACACTCTCTCCTGCAGCTTTATGAAGAAGGTACTTGCT  
TTCCTTTCTGCCATGATTGTAAAGTTTCTGAGGCTTCCAGCTATGCAGA  
ACTGTGAGTCAATTAAACCCGTTTTCTTTATACATTACCAGTCTTGGGCA  
JTTCTTTACAGCAGTGTGAGAACTGCTGGCGATGAGAGTGACCTCTGGTT  
GTCTCCTCACTGCTCATTATATGCTAATTATAATGTATTAGCATGCCAAAAG  
ACACTCCCACCATGACCCCAACAGTCATGCCTGTGCCGGTCTCAGCACCA  
TGACAGTTTACAGATGGCATAGCAACGTCTAAAAGGTACCCCATATGGAC  
TAACAAGGGGAGGAACCTCAGCTCTGGGAAGTGCCCTACCTCGTTCCAG  
AAAGCTTGTGAATAATCCACTGCTTGTGTTAACATATAATTAAGAAATAAC  
TATTAAGCATCCTTAGTTCAGCAGCCCAAGCTGCTGTTCTGCCTATGGAG  
TAGCCATTCTTTATTCGTTACTTTCTTAATAAAATTGCTTTTACTTTAC  
TGTATGTACTCGCCTGGAAATCTTTCTGTACGAGGTCCAGAGCCCTCTC  
TTGGGTCTGGATCGGGACCCCTTTCTGGTAACATTTTGACCAATTTCTCC  
CTTCTGGAATGGGAATGTTTACACAATGACTGTATCACTTTTGAATCTTG  
GAAGTAAATAATTTGTTTTGACTTTACAGCCTCATAGGTGGAAGGAACT  
TGACTTGAATTTGAGATGAGACTTTGGACTTTGGGACTTTTGGGTGGGG  
CTGGAATGAGTTAAAAGTTGGGGGGATTATTGGGAAGGCACGATTTTATT  
TTGCAATATGAGAAGCACATGAGATTTGGGGGACCAAGGGTGAATAATA  
TGGTTTGGATGTTTGCCCCCTCCAAATCTCACATTGAAATGTAATCCCA  
GTGTTGAAGTGAGGCCTGCTGGAATAATGTTTGGATTACAAGGCTGTGAG  
CACATTGGATAAGACGTGTAGGNCCC

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CGCAGCTCGCTGGTTAATTTCTGTGGCTCCTGTGACCACTATTATAGCACC  
AGGTCTATGACCAGGAGAATTAGACTGGCATTAAATCAGAATAAGAGATT  
TTGCACCTGCAATAGACCTTATGACACCTAACCAACCCATTATTTACAA  
TTAAACAGGAACAGAGGGAATACTTTATCCAATCACAAGCTGCTTTC  
CTCCCAGATCCATGCTTTTTTTCGTTTTATTATTTTATAGAGATGGGGGT  
TCACTATGTTGCCACACTGGACTAAAACCTCTGGGCTCAAGTGATTGTC  
CTGCCTCAGCCTCTGAAATAGCTGGGACTACAGGGGCATGCCATCACACC  
TAGTTCATTTCTCTATTTTAAATATACATGGCTTAAACTCCAATGGGA  
ACCCAAAACATTCAATTTGCTAAGAGTCTGGTGTCTTACCACCTGAACTAG  
GCTGGCCACAGGAATTATAAAAGCTGAGAAATCTTTAATAATAGTAACC  
AGGCAACACCATTGAAGGCTCATATGTAAAAATCCATGCCTTCCTTTCTC  
CCAATCTCCATTCCCAAACCTTAGCCACTGGCTTCTGGCTGAGGCCTTACG  
CATACCTCCCGGGGCTTGACACACCTTCTTCTACAGAAGACACACCTTG  
GGCATATCTTACAGAAGACAGGCTTCTCTCTGGTCTTGGTAGAGGGCT  
ACTTTACTGTAACAGGGCCAGGGTGGAGAATTCTCTCTGAAAGCTCCATC  
CCCTCTATAGGAAATGTGTTGACAATATTCAGAAGAGTAGGAGGATCAAG  
ACTTCTTTGTGCTCAAATACCACTGTTCTCTTCTTACCCTGCCCTAACC  
AGGAGCTTGTCAACCCCAAACCTCTGAGGTGATTATGCCTTAATCAAGCAA  
ACTTCCCTCTTCAGAAAAGATGGCTCATTTTCCCTCAAAGTTGCCAGGA  
GCTGCCAAGTATTCTGCCAATTCACCCTGGAGCACAATCAACAAATTCAG  
CCAGAACACAATACTACAGTACTATTAGAATAATTATTATTAATAAATTC  
TCTCCAAATCTAGCCCCTTGACTTCGGATTTCACGATTTCTCCCTTCTC  
CTAGAAACTTGATAAGTTTCCCGCGCTTCCCTTTTTCTAAGACTACATGT  
TTGTCATCTTATAAAGCAAAGGGGTGAATAAATGAACCAAATCAATAACT  
TCTGGAATATCTGCAACAACAATAATATCAGCTATGCCATCTTTCATA  
TTTAGCCAGTATCGAGTTGAATGAACATAGAAAAATACAAAACCTGAATT  
CTTCCCTGTAAATTTCCCGTTTTGACGACGCACTTGTAGCCACGTAGCCA  
CGCCTACTTAAAGACAATTACAAAAGGCGAAGAAGACTGACTCAGGCTTAA  
GCTGCCAGCCAGAGAGGGAGTCATTTCAATGGCGTTTGAGTCAGCAAAGG  
TATTGTCTCACATCTCTGGCTATTAAAGTATTTTCTGTTGTTGTTTTTC  
TCTTTGGCTGTTTTCTCTCACATTGCCTTCTCTAAAGCTACAGCCTCTCC  
TTTTCTTTCTTGTCCCTCCCTGGTTTGGTATGTGACCTAGAATTACAGTC  
AGATTTTCAGAAAATGATTCTCTCATTTTGTGCTGATAAGGACTGATTCTGTT  
TACTGAGGGACGGCAGAACTAGTTTCCTATGAGGGCATGGGTGAATACAA  
CTGAGGCTTCTCATGGGAGGGAATCTCTACTATCCAAAATTATTAGGAGA  
AAATTGAAAATTTCCAACTCTGTCTCTCTTACCTCTGTGTAAGGCAAA

FIG. 3 (26 of 52)

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TACCTTATTCTTGTGGTGTTTTGTAACTCTTCAAACCTTTCATTGATTG  
AATGCCTTCTTGGCAATACATTAGGTTGGGCACATAAGGAATACCAACA  
TAAATAAAACATTCTAAAAGAAGTTTACGATCTAATAAAGGAGACAGGTA  
CATAGCAAACCTAATTCAAAGGAGCTAGAAGATGGAGAAAATGCTGAATGT  
GGACTAAGTCATTCAACAAAGTTTTTCAAGGAAGCACAAGAGGAGGGGCTC  
CCCTCACAGATATCTGGATTAGAGGCTGGCTGAGCTGATGGTGGCTGGTG  
TCTCTGTTGCAAAAGTCAAGATGGCCAAAGTTCAGACATGTTTGAAGA  
CCTGAAGAACTGTTACAGGTAAGGAATAAGATTTATCTCTTGTGATTTAA  
TGAGGGTTTCAAGGCTCACCAAATCCAGCTAGGCATAACAGTGGCCAGC  
ATGGGGGCGAGGCCCGGCAGAGGTTGTAAAGATGTGTACTAGTCTGAAGTC  
AGAGCAGGTTCAAGAGAAGACCCAGAAAACTAAGCATTCAAGCATGTTAAA  
CTGAGATTACATTGGCAGGGAGACCGCCATTTAGAAAAATTATTTTGA  
GGTCTGCTGAGCCCTACATGAATATCAGCATCACTTAGACACAGCCTCT  
GTTGAGATCACATGCCCTGATATAAGAATGGGTTTTACTGGTCCATTCTC  
AGGAAAACCTTGATCTCATTCAAGGAACAGGAAATGGCTCCACAGCAAGCTG  
GGCATGTGAACCTACATATGCAGGCAAATCTCACTCAGATGFAGAAGAAA  
GGTAAATGAACACAAGATAAAATTACGGAACATATTAACTAACATGAT  
GTTTCCATTATCTGTAGTAAATACTAACACAACTAGGCTGTCAAAATTT  
TGCCTGGATATTTTACTAAGTATAAATTATGAAATCTGTTTTAGTGAATA  
CATGAAAGTAATGTGTAACATATAATCTATTTGGTTAAAATAAAAAGGAA  
GTGCTTCAAAACCTTTCTTTTCTCTAAAGGAGCTTAACATTCTTCCCTGA  
ACTTCAATTAAAGCTCTTCAATTTGTTAGCCAAGTCCAATTTTACAGAT  
AAAGCAGGTAAGCTCAAAGCCTGTCTTGATGACTACTAATTCAGAT  
TAGTAAGATATGAATTACTCTACCTATGTGTATGTGTAGAAGTCTTAAA  
TTTCAAAGATGACAGTAATGGCCATGTGTATGTGTGTGACCCACAACAT  
CATGGTCATTAAAGTACATTGGCCAGAGACCACACTGAAATAACAACAAT  
TACATTCTCATCATCTTATTTTGACAGTGAAAATGAAGAAGACAGTTCCT  
CCATTGATCATCTGTCTCTGAATCAGGTAAGCAAATGACTGTAATTCCTCA  
TGGGACTGCTATTCTTACACAGTGGTTTTCTTCATCCAAAGAGAACAGCAA  
TGACTTGAATCTTAAATACTTTTGTTTTACCCTCACTAGAGGTCCAGAGA  
CCTGTCTTTAGTATTAAGTGAGACCAGCTGCCTCTCTAACTAATAGTTG  
ATGTGCATTGGCTTCTCCAGAACAGAGCAGAACTATCCCAAATCCCTGA  
GAACTGGAGTCTCCTGGGGCAGGCTTCATCAGGATGTTAGTTATGCCATC  
CTGAGAAAGGCCCGCAGGCCGCTTCACCAGGTGTCTGTCTCCTAATGTG  
ATGTGTTGTGGTTGTCTTCTCTGACACCAGCATCAGAGGTTAGAGAAAGT  
CTCCAAACATGAAGCTGAGAGAGAGGAAGCAAGCCAGTTGAAAGTGAGAA  
GTCTACAGCCACTCATCAATCTGTGTTATTGTGTTTGGAGACCACAAATA  
GACACTATAAGTACTAGTATGTCTTTCAGTACTGGCTTTAAAGCTG  
TCCCCAAAGGAGTATTTCTAAAATATTTTGAGCATTGTTAAGCAGATTT  
TAACCTCCTGAGAGGGAATAATTGAAAGCTACCACTCACTACAATCAT  
TGTTAACCTATTTAGTTACAACATCTCATTTTGAGCATGCAATAAATG  
AAAAATCTTCTTAAAAAATCATCTTTTATCCTGGAAGGAGGAAGGAAG  
GTGAGACAAAAGGGAGAGAGGGAGGGAAGCCTAATGAAACACCAGTTACC  
TAAGACCAGAATGGAGATCTTCTCACTACCTCTGTTGAATACAGCACCT  
ACTGAAAGAACTTTTCACTCCCTGACCATGAACAGCCTCTCAGCTTCTGTT  
TTCCTTCTCACAGAAATCCTTCTATCATGTAAGNTATGGCCCACTCCAT  
GAAGGCTGCATGGATCAATCTGTGTCTCTGAGTATCTCTGAAACCTCTAA  
AACATCCAAGCTTACCTTCAAGGAGAGCATGGTGGTAGTAGCAACCAACG  
GGAAGGTTCTGAAGAAGAGACGGTTGAGTTAAGCCAATCCATCACTGAT  
GATGACCTGGAGGCCATCGCCAATGACTCAGAGGAAGGTAAGGGGTCAAG  
CACAATAATATCTTTCTTTTACAGTTTAAAGCAAGTAGGGACAGTAGAAT  
TTAGGGGAAAAATTAACGTGGAGTCAGAATAACAAGAAGACAACCAAGCA  
TTAGTCTGGTAACTATACAGAGGAAAAATTAATTTTATCCTTCTCCAGGA  
GGGAGAAATGAGCAGTGGCCTGAATCGAGAATACTTGCTCACAGCCATTA  
TTTCTTAGCCATATTGTAAAGGTCGTGTGACTTTTAGCCTTTCAAGGAGAA  
AGCAGTAATAAGACCACTTACGAGCTATGTTCTCTCACTAATACTATGC  
CTCCTTGGTCATGTTACATAATCTTTTCGTGATTCAGTTTCTCTACTGT  
AAAATGGAGATAATCAGAATCCCCCACTCATTGGATTGTTGTAAAGATTA  
AGAGTCTCAGGCTTTACAGACTGAGCTAGCTGGGCCCTCTGACTGTTAT  
AAAGATTAAATGAGTCAACATCCCCCTAAGCTTCTGGACTAGAATAATGTCT

FIG. 3 (27 of 52)

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GGTACAAAGTAAGCACC\_AATAAATGTTAGCTATTACTATCATTATTAA  
ATTATTTTATTTTTTTTTTTTTGAGATGGAGTCTCACTCTGTTGCCAGGC  
TGGAGTGCAGTGGCGCAATCTTGGCTCACTGCAAGCTCTGCCTCCTGGGT  
TCACGCCATTTCTGCTCAGCCTCCCGAGTAGCTGGGACAACAGGCAT  
GTGCCACCATGCCCAGCTAATTTTTTTGTATTTTAGTAGAGATGGGGTT  
TCACTGTGTAGCCAGGATGGTCTCTATTTCTGATCTCATGATCCGCCT  
GCCTTGGCCTCCCAAAGTGCTGGGATTACAGGCGTGAGCCACCGCGCCCG  
GCTATTATTATTATTACTACTACTACTACCTATATGAATACTACCA  
GCAATACTAATTTATTAATGACTGGATTATGTCTAAACCTCACAAGAATC  
CTACCTTCTCATTTTACATAAAAGGAACTAAGCTCATTGAGATAGGTAA  
ACTGCCCAATGGCATACTCTGTAAGTGGGAGAGCCTCAAACTCTAATTCA  
GTTCTACCTGAGTAAAAAATCATGGTTTCTCCTCCATCCCTTTACTGTA  
CAAGCCTCCACATGAACATAAAACCAATATTCTGTTTTTAAGATAATA  
CCTAAGCAATAACGCATGTTACCTAGAAGGTTTTAAATGTAACACAAT  
ATAAGAAAATAAAATCACTCATATCGTCAGTGAGAGTTTACTACTGCCA  
GCACTATGGTATGTTTCTTAAATCTTTGCTATACACATACCTACATGT  
GAACAAATATGTCTAACATCAAGACCACACTATTACAACTTTATATCCA  
GCTTTTCTGACTTAGCAATGTATTGATGACATTATGCATGCTTAGACCTC  
C

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GTATTTCTATTCTCGGTTATAACACAATCACAGTGATTTGTCATATCTTTC  
CAGGATTTGTTAATTTCACTTCTTCAGCTGTTTCCCCCTTGTGGCTGGA  
ACTGATTTTCTATCTTCTGGGAGAATCTTCAGCAAGCCAACTCAGGATTT  
GTTGGGTGCATTTGTCAAGTCTAGGACCCAGGCTCTGGGTGACTGATTT  
CCTCTAATTACCGAGCAATGTAAATGAGGAAGTCTGATTGTGTAAAGGT  
GTTAAACTTTTGTGTGACGGCAAACTTTAATACCATGAATAGAGATTCC  
AGAATTTTCCAAGCTTCTAACGGGATTCCTTTCCTCCCTGACATTAGAAT  
GTTAGAAAATCTACCACAAAACATCTGTGAGGCTATCCTACAAGGCCCGT  
TTTTCAAAATAGGTTTTTACAAGGATTGCTATTTGGGATGATAGTTTCAG  
AAAGGCGCTATCAAAGTTAATTGATGATGTGTGCAAGCTGAAAGTTATAT  
GTTAGAACTAGCAGTGATTTCAAAAATATCCCTTTTAGGCTTTTTGCTAA  
TATATCTGCTCATTTTCAAAGTTCCCAATATTATAAACTTTTTAAAGCA  
GAAAGAAGAACCCCTCCATTTCTGCTGGCCCCCTTCCCTGTTCAACTAAAAA  
GTATTTTCCCAAGCTTCTAACGGGATTCCTTTCCTCCCTGACATTAGAAT  
ACCTACCATAAGTTCTTTGAAGGGCTCATTCTGAGCGCTTCTGAGTGCC  
TGGGATCTGTTATTTCTCTCCATTTCTGCTGCTGCATGGTAGTCCAAGTC  
CTCCTCCCTTTTCCCTAGGCCATTTGAATCATCTGCTAATTGGTTTTCC  
TGATTGCCACGGAACTTCTCCATCCCTTCTCACATATCAGCCACAGA  
AGTATCTCCAAAAGCAATCTGGTGACATGAAGCCCTTGACAAAACCC  
ATTCAATTCTGGTCCACACCTCCTTTGTGGATAAGTTCAAGCTCCTGAG  
TGTGGCAAGCAGGGCCCACTGGAATCCCTGCCCTCCTCTCCTATCCCA  
CGCATCAATCTTCTGTCTATTTGCAGTTCCTTGAATGTGATATTCTTT  
CTAGTCTCTGTGCTTTTGCATAACCTGTTCTTCTGACTGGAACTCCTT  
CTCCTCCTTGTAGTTTGGCTAATTTCTAGTCTTTCAAGACTCAGCTCATG  
CTTCACCCCTCTATAACAAGTCTTTCCCAAGCTGGGTGGTGGATGCTC  
CTCTGTGCTGTGTGAGTCTTGAACATCCTCAGCAAACCTCAGCTTTGTTT  
GCTTGTCTCCTTGTGTCAATGCACCTGATTCAAGGCTGGCATATACTG  
TTCACCTCCATGACTGGCTCATGGTGGTGCTCCGTGAATATCATCCACCC  
AAACGGATGAGAGCTACCATGCCATCACTTGTGACTTCCATCTGGAGCTA  
ACCTCCCCCGACAGGAAAGCGTTTCTTAGGAAAGAATATCTTTGGGTTA  
AATAGAAGTAGAGACTACCAGAAGCACTATGTCCAGCTCAGAATGAACT  
GCTCAGTAAGCAGCCTTGTCAATGAGGAGGCAGCAGGCCAGCCCCAGAGG  
CCTCAAAGTGGGAGAGTAGAGAAGCGCAGTTCCTGCCACAAAGGCACAGT  
GGACACCTTGCTCCCTGGCTGGCTGGAAGCAGATGGTGTCCACCTGCTT  
CCATGGGAATTCTGCACCTTTAATAAAGTTTTATGGGACAGGAAGGTGAC  
TGGCATTGACATTGTAACGAGGAATGGGTGGTGCCACCTTTGCTGTGTCT  
TACCAGAAATACCTGTGGCAGGTAAATTTCTAGAGAGACCCTCCCATTTT  
TCCCATATAGCAATTTGAAATGTTTCTGAGGGCTTTCCAAATTCATCT  
GGGAACATAGGAGTTCCAGAAAGATGAAATCAAAGGTGATGGTATGCCAA  
AGAAAGTAGCTTTTAGAATGACTTACATTAGCCATTCTCCATTGAGCAC

ACCAGGCATT CAGTTTGAGGGGTGTGTGTGTGTGTGTGCGCGCGCGCGTGT  
CGTGCATGAGTGCATGCGCGCGCGTGTACATAGGGGAAGGAAACAAAAC  
AAAAGTACACAAGACATGATAGTTGTCCTCAAGGAGTTTTTGC AAATGTT  
CACAATTTAAGAGAATATGCTGTGCTGTGGCTGGTGTATAAACCAACTGC  
TAGGGAGAGGCCTTCCACACACACTTGGGGCAAATGCGACCTCTAGGACT  
GCCAGTGGAAATCTGGGCATGCTGTTTGTGGTCGATAAACCCCTGGTCCCTT  
GATCAGGGACCTATGTTTACTTTTCTCTCCCTGGAAGTCTTCATTAGTG  
GGCATCCAGAAGGTCTTGACAGGGCAGAGGGAGGCACAAAGACAAGAGT  
TTGAAACCAGCCTGGACAACAAAATGAGTTTCTATCTTTACAAAAAAAT  
TTTTAAAAAATTAGCCAGGTAGGATTGCATGTGCCTGTAGTCCAGCTAT  
TCAGGAAGCTGAGGCAGGAGGATTCCCTGAGACCAGGAATTTTGAGGCTG  
CAGTGAGCTATTAAGTTGGCGCAAAGTAATCGTGGTTTTTATCATTAAA  
AGTAATGGCAAACTTTAATGACAAAAACCGTGATTACTTTTGACCAA  
TTTAATATGATTGCACGACTGCACTGTGCTCCAGCCTGGGCAACAGAGTG  
GGACCCTGTCAAAAAATAATAATAATAATAATGTAAACATGTAAAAAAA  
ACCCCAAAAAACAAAAAAATGGGTGTTGAGACCCCTGAATTGAGGAATAA  
TAGGAAGGAGTGTGATTCTGTGTGTGCATGCATGGGTGTGCACCCTCAGT  
GCCTGGGTGGCTTACCCTGGGCTAGTTTCAGGTGGCAAATGGTTTTCTCC  
AGCTGGGCTACCACCATCTTCCCCAGGGCCTGTCCATGTATTTGGTGGC  
AAGATACCTTAGGACTAGAGTCCCTCCTCAGAGGAAAGGCTCCTCCCAT  
TCTCTGGCTTTAGGTAGTAGTCCATGACTTCAACAGGTCCCCAGTGCAA  
TGTTATGGGTAGTTTAGGTGGGGTCTCCTCTGAGAGCCTCCCATAGCCC  
AAAAGGCCCTGTCTAGCTGGCACTGCATCTCCCTCTTCCAGCTCTCAG  
CCTTTCTCTTTGCTCATCCCACTCCGCACAGGCTTTCTGCCTGATCCTTG  
GATGTGTCAATCCTGCCCCTAAGGGATGCAAGGCAATTTGTCTTTTATT  
ATTAAGATCTCTCCTGAGGCCACGTGTGGTGGCTCACACCTGTAGTCCTA  
GAACCTTTGGTAGGCCAAGGTAGGAGAATTGCTTGAGCTCAGGAGTCCAG  
GCTGTGATGATGACCATGATTGCACCATTCATTCCAGCCTGTGTGACACAG  
CGAGACCCTGTCTTTTTTCTTTTTTTTTTTTGGAGACAGGGTCTCGCTCTGT  
CATCCAGGCTAGAGTGCAGCGGTGTTTTTCTGCTCACTGCAGCCTCAACC  
TGCACATTTTTTTGTAGAGACGGTGTCTTGCTATGTTGCCCAGAGTGGCCT  
CAAACCTCCTGGGCTCAAGAGATCTTTCCACCTCAGCCTTCCAAAGTGCTG  
GGACTACAGGCGTGAGCTACCGCGCCCAACAAAGACCCTGTCTTAAAAAG  
AAAACAAAAATAAACAACTCCCTCAAGTCTTTTTTTTTTTTTTTTGGAGCGG  
AGTCTCGCTCTGTGCGCCAGGCTGGAGGGCAGTGGCGCAATCTTGGCTCA  
CTGCAAGCTCTGCCTCCCGGGTTCACGCCATTCTCTTGCCTCAGCCTCCC  
SAGTAGCTGGGACTACAGGTGCCCCGCCACCACGCCTGGCTAATATTTTGT  
ATTTTAGTAGAGATGGGGTTTCACTGCGTTAGCCAGGATGGTCTTGATC  
TCTCACCTTGTGATCCGCCCCGCTCGGCCTCCCAAAGTGCTGGGATTAC  
AGGCATGAGCCACCGCGCCAGCCAGACCTCTTGAGTCTTAACTCCTCT  
GTAGTTCCAGCCACCTTTAGCACATGACTCTGTAAATTTTGTCTCACT  
GTCTGAAATCATCTCCTGTCCACTCTTGACTGACAGGTCTCTGCACTAGC  
CCACTGCTTAATCAGAGTAGGTCCCTGTCAACTTATTCATATTGTGTCCC  
CATGCCAGTGTGGATGATTAAAAATTGTTGAGTGGAGGCTGATCAGATGAG  
CCATCTCCTTCCAAGTCCCTCACTTGCTGGCTCCTGTCTTAGTTTTAGTCC  
CCATTCTTCAAAGAACGTGAGCCCTGGAAAGTATTTTAGTCATTTAGTTC  
AGTGCCCTTTGGATGGGAGGATCACATCCCTGGGTCCCGTCTGCAGACTG  
TTTTGCTCTAGCTGACTAGGCAGGATCCCTGCCTTCTCTCACTTCGGCA  
TGGGACTTCTTTCTGAAATTGCTGCTCAGTCAAGAGAATGACCTTCCCA  
ACATAATCTACTCCACAGGGACTTAAAGGTGTGTGAGAGATCTCTTGCT  
CATCTTTCTGGCCAGGTGCCAACGTGAGTTTATAGCCAAGGGACAAGACT  
AGTTAGCAGATCAGGCAGGTCTTAGACCCCAAGCGTAAGTGCCAGACTTCT  
AGCTGCAGTTGTTCTGCCCCACTGGGCGTTTCAGGTGGAGAGAGGGCAT  
GGCACTACACTGAGCTCTCGGCGAAACCCAGGACTCTGAAATCTCGGTGT  
CAGCCACAGGCCACTCTTTTCAGCAGGACTTCAGTCAGTCCTGTCACTAG  
GCTGTGAGACATGGTAGGCTTTACCCC

>Contig35  
AAGGAGTGTGCTTGCTGATAGCATGTGTGANGGGACGAGGAGTAAATAAT  
TTCTGCCTTCAAGAAATTGCAAACTAGTAATGGAGATAAAATCAACAGAG  
GAACAATTAGAGTATAAGGTAAATCTAAGGGCCATAAGAGAGGAGAAGA

AGTATGGGAGTTT CAGAGG T AGGGGGTAAATGAGGGGAGTAGGTGGGTAGA  
AAAGGTTTAAAGTAAATAATGATGGGAAGGAAGACAAAAAGACGACAGGG  
GTGCCAAAGGACTCTTAACCTCATCTGAACGGAGTTGCCCTGTTTTGCTC  
TCTGATGCTCATGTATCTATCCTTAGAGACAGCTTGGCGGGCAATGTAGA  
GCGTAGGGGCTGACATAGGGGGTTGGAGTCCACCTCCGTGACTTCTAGC  
AAATTAGCAAACCTTTGCTGCTGCTAAGCCTATAAGGCGGACAGAAATGCC  
ATCTTTAAAGCTTGTATGTAAAGTGCTTAGGACCTCGTAGGCATCAACA  
GGAATAATGGATGAAACAAAAACAACGGTGCGTATCTTGGAGAAAGTGGCA  
TCTGAGCAGGAGTATTTTGAAAGGTAGGAAAGGGCTCCAAGCACATCTAA  
GAGATTAGGGAACGCAGAAGCCTTAGCCCTGGGTGCAGATTTAACCAATC  
AACTTCTAACCAACCGCAGGCTGAGAGGTGTGGAGTGAGAGCCCCGCCAGA  
GGCAGGAGACCCGGGCTTCGGCCAGACCCCGCCTCCTGGTACAGAGGACC  
ACGCCCCGGCTCTGCCTGGAGCCAAATGTGGATCAAAACAGCGCGCAGCTT  
CCCCTGCTGGTGA AAAACCCGAGCAAGGGGCCTCAGTTTCTTTATCCGGA  
ACGTGGTGACAATGACATCTCTTTGCAAGGCTGCTGCAGGGCTTTCTGGA  
AATACGCCCGTGAGGTATCTGGGCCCTGCGCACAGCCTCCCCGCGCCAGGA  
CCCAGACGCTACTCTGGGGTCCCGTCTGCGCTCCCGGGATGGAAAACGC  
CCAGGGGAAACTTAGGCAGCGCAGCGGACGGGCACCTCCCGCGGACCAA  
CTCACTCGGTGGCCTCCTACTTCCCCGGCCGTGTTCCAACGCTGAGAAT  
AACGGGAACAGCGGTCTACTCACCGACAGCGGCAGCAGCGGTAGGCCCG  
GGCCCCACCATGACTCTTCAGTGACAGTTTTTCTTCAAACGCCGSCCTG  
TAGCCAGGACCGGCGTGCCGCGCGTCCACGCGTCTCATTGGCTCCTGCG  
GGTTTGAAACTCGCTAGTCGTGAGCAGGGAGGGCGGGACAACAGGCAAT  
AGGCTCTTTGCGGTGGCTCTGGCCTTGAGAACCCGACCTTGGGGCCCTT  
TGATTGGAAGAACGTGCAGCGCACCTCGGCATTGAGGGCGGCTTCTCGG  
GGCGCGGCGCGCCCGCCTCTGAGTGCGCCTGTGAGTGCGCCTCCGAGTG  
GGCGTGGGACCCTCCGTGGGGGCTCAGCCGGGCTGGTGGTTGGGGGGCG  
GTTACGCTGAATCCAGCTGGGGTTGGCGCGCCGGGAGTCCCTGGGCGGAG  
AGACAGGGCGGTCTCTCCAGGATGCTGGGGCCGCTACCTGATTCTGTCT  
TTCAAAGTCTCAGACTCACAGGAGCTGTGAAAAATAATATTATAAAGAG  
GACATATGGGTCTTATGCATCTAAAGGCTCCTAGTTCTTAGTACTGCAGG  
GTGGCTCGTTTAAATTGTGGTAAATATGCATAACATCACATATACCATT  
TAACCATTTTAAAGTGTTAAATTTTCAA AAATGTGCAGTTTAGTGGTAT  
TAAGTACCCTCACATTGTGGCACAGCCACCCTACTGTCTTTCCAGAAC  
TTTTTCATCTTCCCAAATGAAACCCTGTACCCGTCACTAACTCCGCACTC  
CTCCCTCCCCCAGCCCCAGGCAATCACCATTCTAGTTTCTGTCTCTATGG  
ATTTGACAACCTGTAGGTGCCATATAAGTAGAATCATGCAGTATTTGTTCT  
GTGACTGGCTTGTCTTCACTTAGCATAAAGTATTCAAGGTTTATCCATGTG  
TAGCATGTGTGAGAAATTTCTTTTCTTTTAAAGGGGAATAGCATTTCGTT  
GTGTGGAGATGCCACATTTTGCTTCTTGGTCCATCCCTCTCCGGACACTT  
GAGTTGCTTCCACTTTTTGGCTATTGTGAATAATAATATGAACATGAATG  
CACAAATAACTCTTTGAGACTCTCCTTTTCACTTTTGGGTATATACCA  
CGAAGTGGTATTGTTGGATCAAACGGCAATTCTATTTTTAATTTTTTGAG  
AAACTGCCTTACTCCTCTCACGGTGATCTCTTGTTCAGGTATATTTTCG  
ATTTACCTGATCAGCTGACTATAAGGCCATAAGGCTAACGGAGAAACGC  
AGGCCTAGTTTCTCCTAGTTACTAGGAGATCGCAGGCCTCGTTGTCTGA  
ATCCCTAGACACACTTCATTCCCCTTGTTTTAATCCTAAATTTTTTTCT  
TTTGAAGTTTGCTCTGTTTCATCTATTCTCCAGTTTCTTAAAGAGGTCTG  
GAAAATGCTTTTGGCTCCTTGTGTATGAAGGTTCTCTTCCATGGATGCT  
GGAGAAGTCTGTGTGGAGGGGCAGTCATATCTGGGCACCTGTTGGCCAG  
GTTTCAGCTTACCAGTTGGGTACTCAGCAGGGCATGAAGCCACTGCAGCAG  
CCCTTCTCTTTAGCCGTAATAAGGGAGTTTGAAGAGAGCCAGGGTTTCT  
GGATTTATGCATTTTGATATTTTCAATAGTGTATTAAATGTTTAAATAG  
GAAAACCTGATCATTATTTTTGTTAATGACTGAGAAAGGACTCCTTCACC  
AACAGTTTCAGAAAAGTGAAGGCGGTTTTGTTTTGGTCTTTGTAGAATCT  
AGGTGGTTGAATGCATGTGAGTTGTAGAAGTCACCTTGCTGATATCCCA  
CGCAGTGCTGGAGTATTCACAGACCCCATGTAGGTACTGCACCTTTGCA  
GGTATACTGTGTTGGTGGTGAGCTGCCTTACCTGTCTGTTATTGGAGA  
CCCTGCTTATTAGGAAACTTAAATGAAGTCAAAATGAGCTTCTTGCTT  
ACTGGTCTAGTCTTTTGGAGCAACATAGGCCAGTTCTGCCTCGTTTTTT

FIG. 3 (30 of 52)

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TCCATCCTTTGGGTATTTGACGGTCTATTTTGTAGGACACAAAATGTGGG  
AAAATAGCTAGGCAGGTTTAAAAATTCTCAACTCTACCAAGCATGGTGGC  
TTATGTCTGTAATCAATCCAGCACTTTGTGAAGCTGAGGCAAGAGGATT  
GCTTGAGCCTAGGAGTTTGAGACCAGACTGGGCAACATAGCAAGACCTCG  
TTTCTTAAAAAATAAATAAATTACAAAAATTAACCAGGCATGGTGGCA  
CACACCTGTAGTCCCTTCTACTCAGGAGGCTGAGGTGGGAGGATCACTTG  
AGCCCAAAGTTGAAGGATGCAGTGCAGTGTGGTCATGCCACCGCACTCC  
AGCATGGGAGGCAGAGCAAGACCCTGTCTCCAAATAAATACATAAATTAA  
ATTCTTAACTCATTATCAAGATATCCACTGTAGCTTTCCATCATCCTGG  
TGTGTGTTTTTTTGAAGGATCTGGCTCCATTGCCCGGCTAGAGTGCAGT  
GGCATGATCTCAGCTCACTGCAGCCCCACCTCTCTGGCTTAAGCGATCA  
CCCACCTCAGTCACCCATCTGGGTAAATTTTTGTATTTTTTGTAGAGATGG  
GGTTTTGGCATGTTGCCCCAGGTTGGTCTTGAACCTCTGGCTCAAGCGAT  
CCATCTGCCTCCATCTCCTAAAGTGTGGGATTACAGGTGTGAGCCACCA  
CACCAGGACAATCCTGGTGGCTTTTAACGGTTTTCCATTGCTCTCAGGCT  
AATGACCTATAAGCCCCCTGCGGGCTTGGCCTTTTACTCCCTEAGCATTAG  
CCACCTCCCTTAGCCTTAGCCCACTACTCTCCCTTGCTCAGTGTTAT  
CCAGACACTTTGTTTTTTCCTTTCCTACTCTCTGTCTGGGAATCCA  
ACCTTTCTTCTCATTCTCTAGTTGATTATTATTATTTTTACTCTAGCA  
GCCTTATTGAGATTTACATACCGTACGATTCTCCCACTTACAGTGTAC  
AATTCAATTTTCTAACATTTTCATCACCCTTAAAGAAACCTATACTCA  
TTAGCAGTCACTCCCCATTCTCCCTCTCTCAGCCCTAGAAACCATGA  
ATCTACTATCCATCTCTATAGATTTGCCTTCTGGACATTTTATATGTATG  
AAATTATGCAATTTGTGGTCTCTGATGGGCTTCTTTGTTACCAAAATAT  
CATGGGTTTGATCTAGGTCTGTCTGCTGCTGCACAGAAAGCCAGCCACT  
GAGATGACAAGTATTGCCAAGGAAGAAGGCTTTAGTCAGGTGCTGCAGCT  
GAGGAGATGGGGCTCAATCTCAAATCCATCTCGCTGACCTAAAACAGG  
GGTTTGGATAGCAGGGAAGAAATGTAACAATGCGTAAGAAACAGGAACC  
AGGGAGGGGCAAGGAAGCAATCCTGATGAATGAGTGGTCCAAAGTCTCAT  
TGCCTGGATGTGGTATCTGGCGAGTTTCAGTTCTTTGATACTTTTTTTG  
AGAGGCCTGAAGTCTTTTCCCCAGGAAGGAACCTCAAACAAAACAAATACA  
AGCTTCCAGCTTTAAGACCAGAAGCGTCAATTTCTATGTTTATCCGAAAG  
AACAGTCTATGGGACTATTGGTTAAGTTTCACTTTCACTTAGTATGCTGT  
TTTCAAGGTTTATCCACATAGCATGTGTGCTAGTACTTCATTCTTTTATGAC  
TGGGTATTCTATTGTGCGGATATACAATATTTTATTGCCATTATCAGT  
TGATGGACATCTAGGTTCTTTCCACTTTTTGGCTATTATGAATAATGCTG  
TTATGAACCTTTCATGTATAAGTTTTTGTGTAGACATATGTTTTCAACACT  
CATGGGTATATACCTAATGAGAGGAATTACTGTGTACATACGATAATCTA  
TCTTTAACCAATTTGAGGAAGTCCAGACTGTTTTCCAAAGCAGCTGCAGC  
ATTTTACATCTCTACCAGCAGTGTATGAAAGTTCCAGTTTCTTTACATCC  
TCAACAACACTTTTATTGTCCATCTTTTAAATTACAACCATCCTAGTGG  
TTGTGAAATGGTATCATTGTGGTTTTTTATTTGTATTTTCTTGATGACT  
AATGATGTTAAGCATCTTTTTATGTGTTTACTGGCCATTGTATATCTCT  
ATTCAGAGTCTTTGCCAATTTTTAAATTGGGTGAGTTGTCTTCTTCTTTT  
TTTTTGTAGATGGAGCCTCACTCTGTTTCCCAGCTGGAATACAGTGGTGT  
GATCTCAGCTCACTGCAACTTCCACCTCCTGTGTTCAAGTGATTCTGGTG  
CCTCAGCCTCCCAAGTAGCTGGGATTACACGCACCTGCCACCATTTCCAG  
CTAATTTTTTCTTTGTATTTTGTAGTAGAGACGGGGTTTCAACATGTTGG  
CCAGGCTAGTCTCTTTGTTGACTCTTAACCATCCTTCAGTCTCAGACAAA  
ACATCCCTTTCTCAAGGATTGTGATTAGCTTGATTATTTGCTTATCTTTC  
TCCCTGCTAGTCTGTAAACTGAGGGTAGGCCACTATATTCATTGTTCTTG  
GCACCAAATAGAACTAAATTAATGTCTTTTGAATGAATAGGGCTTTCTC  
CTTTTAAAGATCCCTTCAATACAGTAACCACACTATATATAAGTAGCCAC  
AAGCCCATTCATAATACTACTAGTNCTTGGGCCAAACC  
>Contig36  
GGCTCAGCGTTACTATACTGGTCTCAAACCTCCTGGGCTCAAGCGATCTGC  
CCCCCTCGGCTTCCCAAAGTGTGGGATTATAGGCGTGAGCCACGGTGCC  
TGGCCTCAAATAACTATTTAAGTGAAACAAAAGTATGGCACTAATGA  
AAAATGTATAAATCCATAATCGCAGAGGGATTCAACTTACTTCTTTCGA  
TTATGTAAGGTCAAACAGACAAAAGACAATGACAAAACCTTAATGCAATG

FIG. 3 (31 of 52)

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AACACTTTTGATTTAATGAACATATATTGGATATGTACCCAAGAATTAGA  
GAATACATACTAGTTTTGAGTTTATGCAGAACATTTACAAAAATTTAGTG  
GAAGCCTAAATTATAAAAAGTTGCTGTACGTAGAATAACACACAAACCC  
CTGAGTCCGGAATTCAAAGCCCTCCACACTCTCCTCTACCTTTGCATCTT  
TATCCTCCACCACACTGCAGTGCATACTCTGGGCTACTACTCACTGTTCT  
TGATTCAAATTCATGTTCTGTCTCAGCTCAAATCATTCTCTCTGCTGGAA  
TAAGTACTTTCATACATATTCTGCTATTGAATTCCTGTCTTAGCACCCCAT  
CTACTCCAGACGATGTCCAGTTGGGGTTACTCCCTGTCCCATTTTCTTT  
GATTACACTTTTTTTTTTCTACTTCCATTATATTATTGATCACATCTGTGC  
CACAGTTTGTGACTTTGTGTCTGCTTTTACTCTTTTCTAGACCCCTGATAG  
CTCCTGAAGGGTTGGGTCAATTTCTTTTATTGCTCATTCTCATGGCA  
CAGTGAGTGCTTAATAAATGGCTATTGACTGAAATTAACTGTATCTAAA  
TGGACATATTCCACTTCTGGGCCATTCAATCTTTCTTTCTATTGGAACCA  
GGAGATGGGGAACCATAACAAAGGTAAGGTTGTGCCATGTGAAAGAACAT  
GGAACCTTCCCCTGAGGGCCAAAAAGAGCAGGGAAAGGTGCAAAGACAA  
AATCTTCCATTTTTTAAACAATGTAAGAATGTGGTCCACCTCATGCTCAGG  
TGGGACTTTATCATGACGTTATTTTGGGGACTTATAGCTGCATCATTTA  
CCCCATATACATTTACCTTTAGTGTAGGGAACTGAGGACAGGAATTTTGT  
TGATGCAGACTCTTGTCTAATGAGGCTAACACTTGGAGAATTTTATCATG  
CATTCAAGAAGCTTGTTTTACATTTCTTCAATTAATACTTTAGTTGGTGGT  
TTAGCTTTAGTTGTAGGCTTATCAGATATTTGGAGATATCTTCATRAACG  
ATGGCTTTTGGTTTGAAGAGTTATTCTGAAGCTACTATTTCTGGCAATA  
ATCAAACAGCATGGCCATTTGTTTTGTAAGGCCTTCTAGAAATATGACG  
GTAAATCTACGTGTGGAATAATGCTTATTCTTCTGTCTCTATAAATGT  
GAATCTAGTTTGTCTTCAAATGAAATCAAGTGATTAAATGTAGTTTTT  
TAAGAAGATAAATGGAGCAAGCACTCTGTGTTTACAGTGTGGAATC  
ACTCATCCCTCATAAACTGTCCCACTGATCCTGACTCACATGAATGAA  
TTAAATAAGAGTTAATAACATCAATTTACATTTTAAAGACACTTTCCC  
ATGTTTTAGACTATTGGTTGGAAAAGCTGGTAGGTGTACAATTTGTGGAG  
AGTTGGCTGTTTTGTCTGTCTGTTGTTGACGTATTTCAAAGCCATATCT  
AATTTTGTGTCAGAAATGGTCTGAATCTACAAAAATGTTGAGTTGTGTAG  
TGTGGAGAAGTACGGAGCCATTTACTGAAAGGCTGGGGGAAATGACGAG  
ACCTGAGATAAGGCAGTAGTGGTGCAGACAGAGTGGAAGGGAGGTAGTT  
GAGATATGTTGAGAGTAGAATCAGAATGGACATAGTGAACAACCTGGATGC  
AGGTGGGGGCTGAGGAAGCAAAGTTGAGGATAATTCTGAGACTTCTAGGT  
TGATCCACTGAAGTTACATTATTCAACACCACAAGGAACTAGGGGAATG  
AGAAGGCATACCTGTTTTGCTTTGGAGTGGAAGGGCAGTGATGTAAGAGGA  
GTTAATGAGTTAAAGTTTGGATATGCCTGAACCTCAATTTGATATGTGCA  
TCTGATATACCTTGGGGTGACCCTCCAGGCAATGGTTGAACATGTGTAT  
TCTTAGTAAGTATAGGCATCACAGACTCACATCAGTAAGGAAGCAACA  
GCAAACTTGATTGGACGATATACCTGGAACCTCAGTACCCTATGACTGGAG  
CAAGTCTCTGTCTGAGTGAATGAGGATAAGAAGAATCTTGACCTTGTGGAA  
TATGTTGTTAGGAATATATGTGATGAACAACATAGGATACTTCTACAGG  
GCTCCACATGTAGTAAGGGCTTTATAAATGCTTGATAAATATTATTGTTG  
TAATTTATTTCCAAAGTAAGATGCCACTGGAGGAATCTTTGGAACCCAAA  
TTAATAACAAATAGGACTGGATGCAATGGCTCACACCTGTAATCCCAGCA  
CTTTGGAAGGCCAAGGCAGGAGGATCTCTTGAGCCCAGAAATTCAGACC  
AGCCTGGGTGACACAGGGAGACCTTGTATCTATGAAGAATTAATAAATAAT  
TAACCAGATGTGGTGGTGCACGCCTATAGTCCCTGCTGCTTGAGAGGCTG  
AGGTGGGAGGATTGCTTGAGCCCATGAGGTTGAGGCTGCAGTGAGCCATA  
ATTGTGCCACCACACTCCAGACTGGGTGACAGAGTGAGACCTATCTCAA  
ATAAATAAATAAATAAATAAATAAAGTACAAACCAGCAAACACTAAT  
CCTTTCTAGAGATTATTGAACTCTGGAGGGCAGATCTGAATGGAGCCAGC  
AGAGGGACCTATGGAGATCAGCCTGGCCCTGGACAGCACCAGGCAATGGG  
GTTGCTAGAGAGGTAATGGGGTTGAACAGGGTTTAAGCCATGAGGTCTCA  
AGAATCCGTGAAGACTCAGACTAATTTTTTTTTTTTTTGCATGAGGATTAG  
GTGTTCTAGGAATTTCAATGAGAGCAGGGTTAATGAAGGAATGCAGGGT  
AGGAGAGCTGAGGGAAGGCATCTGAGAGAGCCTGGCTTATGAATGGCTGC  
CTCAGTATGGCTCACCTGCTTCTCTTGTATCTACTTAGCAGATGATCCCA  
CCCCAGGCCTCCAGGGCCAAGGTCATTTCCACATAGTCATGGGCCCTTGA

FIG. 3 (32 of 52)

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GGGCCCTGGAGCAGTGTAAAGGAAGACAGAGTCTTAAGAAATTGCATTAAAC.  
 GTCATGGTGCTTGGCAAGTGTCTGTCATCCTATGCCAAGCCTGATCTGAAG  
 GGGTGCATGCTCATAGGTAGCTGCTGCCCAAGATTACAGCAGCTTCTTCA  
 ATCCCAGATCCATGCTCTCTTATATTCAATTTTCCAGGGGTTCTGTCTT  
 TCGACAGTGATGAGATGCAGAATGACTTATTGAGTTATTCTCTGATAGT  
 TGCCAACTTTTCCAAATGACAATGGGGCATGGAGCTTGAGAGTGGAATG  
 AGGCCCTAGGGATAGCGTGCTTAGGAAAACACTCCCAGCCTGATGTAATT  
 CTGGGGGTACAATGGCATTTCATCATCAAGACTGATGTAAAGGGTGACT  
 AGCAGTGAGTTGGGGGTGACTCGCACTGGGGCTAGGTTTCTGATTCTGCC  
 TAATCCAGACAGAGCAGAAGCACTAGTGGGCTGGTAGAGGGCCTCCAGGG  
 CCTCACTTAATGTCTTGGAAAAACAGCTCCAGATTGTTGGTTCACGTTCT  
 GAGGACAAGCTTGGGTACTACAGGATAGAGAGAGTGGTGGGAGATGCCGT  
 GGCCTGCCCTGCTGATGCCTGCCCTGCCATTCTGCGTGTGATGTCTCTG  
 GGGCATCTTGCCCTTCCCTGCCCAGACCTGTAGTTTCACTGAGGGCATGTG  
 GAGGCCAAATGGCTTCTTAGAGTGTTACTTTCTTGAACAGCTCTGCTGG  
 GAGAACTGGAGGAGCTAGCTAGTCACGGTAACTGCAGCAGTCAAAGGATC  
 GTCCCGGTGGAGGTGGGGTGGAAAGGTAGAGAAAGAGAACATATAGCGTT  
 TTCTTGGAGATGTGTGGGCATGTATAGAGGAAATACCCAATTCCTGAG  
 CCTTGAGCCCTCCAGGAAACCTTGAATATTAGGTTAGTCATCCCCAAGG  
 AAGTCTAAGAATTCTGGTCTCACCCATCTCCTTTAATTCACCAATGATC  
 CTACATGATATTAAGGAACACGGGCCAGTAACCTCCAAGCAATGGATGT  
 GGTGGTGAAGTTTGACCTCATGATGGAGCGGAGGTGGTTTGAACCTAA  
 GAATTTAATTTATTGTTTCAAACCTGTTCTCCACTCAGCGTTATTAAAGCA  
 TACATAATTGACACATAAAAAATTGTATATGTCTACGGTGTACAATGTGAT  
 GTTTCGATCTATGTATACATTGTGAAATGATTACAACAAGCTAAATAACA  
 TACCCATTTCATCGTGTTCAAAGGAATTAACTCAAGCACAAAAGAGAGG  
 TGCTGTTGAAGAGTAGGGCTGCTCTATCTAAGTAGTATGTCTGGGGTTGT  
 CCTGGATCAGGGTCTTTTGTGCTAGTAATAAACAGCCCTTCTGGGGCT  
 GCTCCACTTTCCCCACATTTTCTTCTGGAGCCTCCCTAAGAATTAGGACA  
 TGGCCACTTTCTCTGATAGGCTTCTACTTCAACAAGGACAGGGCTTGT  
 GCTGCCCCATGCCACTTGAGTGTCCCTACAGCACAGAGCTGAGTGCACAC  
 TGGCTGAGTGAGGAAATCCCCCAGATTAATCTTGGTTCTAAGCATCATGG  
 CTGTATTTACACGTATATGAATTACAAATTACAGCATAGTCGAATAAGG  
 ATTTTGTGCTACAACCTGGAATCCAGATTATGCAATTGGATAGTATAA  
 TATTGAAATTCCTAGGACTTTTATTAGTTTTAAAAAATTATACAAGCTT  
 AGAGTAAGAAATTAAACAGTGCAAAAGAATCACTGTGAAAAGTAAATG  
 CTCTGCTCTCTGCTGAGAGACAGATATTGCAGCCCAGATACTACTGGGGTC  
 AATAGTTTTCTTTAAGCATGCCATTTTGATGGTTTATGGGACTTACAGCT  
 CAAGAAGCTTGACACTAGGGTTGATCTCAGAAAATCATTGTTGCAGGTAT  
 TAGATATGACCGTCTCATAAAGATACACACACAGACACAGCGATTGGAGA  
 TATTCACTGGGGCTTATGGGCTGCTTGTCTTTCTGCTCTGTGCCTAAGT  
 TGGGCTCAGAGTAGCCTGGCATCGGCTGTGGGGAGAATGCTGGCATGGGG  
 TTAGCAGGAGCCCACTTAACATGTCTAAGCCACCTGGAAGAGTCTTTCA  
 AGGAGACCAGACTCCAGAGGCCCTAAGGAAGGAAGGACTTTTGGCCGTTT  
 TTAGGTATTCTAGTCCAGAGTTTAGGGAGGAATGGTTTGGCTTTGGGTC  
 GTGTGCCCTTTACCGAGTGGGATGGGATGTGCCATGAGCTGTTGAGCT  
 GGCTCTTGGAGAAGACAGCAAAAGCGGGAATAAGAGGTGAGGAAGCTGTG  
 TGGTTGTAGGAAATCCAGCAGAGGGCCTGGGGGTCAAAGTGGTCATGG  
 TAGTGACGGTGGAGGCTGAGGTGGTAGAAAATCAGAGGACAAACCCCATG  
 GGCTGCTGGTGATCTGACCGAGCTCCTATGCTCTCTGGTTTCAATTTAGG  
 CTCTGTAGCAGCAGATGATTGGCTGGTGTGAGAGCAGTGACCTGCCATA  
 TCAGGCAATCCAAGACAAGTCCAAGCTACGCTGGGAGGAAACCTGAAGGC  
 AGCAGCAGGTAGACTGGCTGAAGACAGACAGGCAGGCAACTTGTCAATCA  
 GATTTGTGTTTTTAAGGACTTTTAACTGGGGAGCCCTCCGGACAGATCA  
 GATGAGAGTGAAATGTGCTCCGCCTTAGCC  
 >Contig37  
 GGGCGTTCCGCAATTCTGTAAAAGGGAGAGTGGTTTTATTATTTTAAAC  
 ATAGTCAAGCTGCTAAAGTATATGATATGTATAGATAGAGTATAATTAA  
 TACTTTCACTACAGACAAATCAGGAGAATGGAATTAATAAACAATTTA  
 CAAATGGGTAAATGGCAGCATTGGGTTGCGCCACCCACGAGAAGGCAGAC

FIG. 3 (33 of 52)

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ACCAAGATTCTAAGATCAACGTTGGCCAGCACTTCAGACTTCAAATAGAA  
TTCGTGATTATGCATTATTTTTCTCGGAAAGTTTTCACTTCACTATATGC  
TACTTGACACTTGCTTTTCTAAGACATCCCTCTATTTTTGAGATGACTAA  
CTCAGCAATTCATTTCTCTCAGCATAAGCTGTCACTCAACCCAAACCCA  
CCAAGCCTGCATTCTACCCTCAATAAGGTCTTGGTGTGTAACTGACCCA  
CTTCACCTAGTTCCCTTAGCCCTCTCTTGACCAGACATGACTCTTTCATAA  
GCTAGACCTATAAAGTCAGGGCTCTTAAGTAGCTGATCTCTGATAGTGCC  
AAGTGTCCCCCACTGTTACATTTTCCACTCCAGCTTCTAACAGGTGATA  
GACTGCTTTTTGGGGTAGGGGCACCAAAACATATAGACCTCATGTTTGG  
ATGTAGACACTCCAGTTTCTTTAAATTACAACCTACATATTAATAATGACT  
TCCAAGTGTACATTTAGTCCAGATCTCTCCCTGGATCCCCAAACTTTGT  
AAAACCCACCGCTAGTTGATATCTTTTGATGTCTGACAGGCATTTCAA  
TTTAATACTGTCAAAACAAAGTTATTGATTTTCATCTCTGCATCTGTTA  
CAAATTTTTCTTACTTTGGTAAATAGCACCCCAAGGCTGTGTCACTGCCAA  
GAATTTCCACAGCTCTTGAATAAAATTCAAATATTTTTCCAAGGCAGA  
AAGGCACAGTGAATCTGGCTCCTGCCTACCTCTCCAACCTCGTATCACA  
CTAGTCTCCCTCACTCACCCCTCCAGGAGCTCAGGTATCTTAAAGT  
TTCTTTTCTTTTTTTTTTTTTTTTTTTTTTGAACAGTTTGTCTGT  
GCCCAGGCTGGAGTGAAGTGGCATGATCTCAGGTCACTGCAACCTCCGCC  
TCCTGGGTTCAAGTGATTCTTGTGCCTCAGCCTCCAAGTAGCTGCAATT  
ACAGGCGCGTGCCACCACACCCGGCTAATTTTTGTATTTTAGTAGAGAT  
GGGGTTTTCAATGTTGGCTAAACCGGTCTCAAACCTCTGACCTCAAGTG  
ATCTGACCACTCAGCCTCCCAAGGTGCTGGGATTACAGGCGTGAACCAT  
TGTACCCCTGCTCTTGAAGTTTCTTGATCCAGACTCATCTGCTTAA  
GGTCTTGCATCTTCACTCCTCCCTCAAATGACACCTCCATGAAGACGCA  
ATTACCTGTAATTACCGTGTCTTATTTAGTCAATGTGTTGGTTTTCTGTC  
TCCTCCACTACAGTGTAAAGCTCTATGAAGGCAGAAACCTTGGCAGTCCAG  
TTCCCAGCACAGTGCCTAGCACACATAGGTATTTAATAACACACAGTAAA  
ATTCACCTTTTAGTGTGCAATTCTGAGTTTTGACAAATGCATCAAGTCAT  
TTAAGTCTGACTATTATCAAGCTATAAGATGGTTGCAACACTATCACTAA  
TTCCCTCATGCTCCTTGGTAGTCAGTCTCACCCCTAACGCCCCCTCCTG  
GCAATCACTGATCCGTTTTTGTCTTTATAGTTTTGGTTTTTCCAGAATG  
CCAATAACTAAGTTTTGAATGAATGAATGCTATTAACCTCTCATTTCTGAC  
TCCAGAGCAACATCCATGCAATATTTATTATTCAGCCCCAAATACTGCC  
CCCTCACCTTCACTCCAACCACCTACTTGATGATACAAGGTGAGACATTT  
GGCATGTGCTTCCCTCATGTTCCCTAGCATTTTCCCTATCTCCTTAGCCTT  
CCTTCTAATCATAAACGAAGAGTGAACCTTCCCTTCTAAAGGCAACTTA  
CTCCTAGGACCTCGATGCCATAATTTGTTTTCTCTAGTACTTTCTATATA  
TACACCAACAATTAGCTCCAGAAAGGTAAAGACTCACTGTGTGCTCATC  
ACTGTGTCTCTAGCGCCTGGCACACTGCAGGTGCTGAAGAAACACCTAC  
AGAATGAGTGAATGAATCTCTCCCTCTCTAGACTCCTTCTCTTTTGTAAT  
CAAACATGTTCAACCTGCAACACAGTCTTATGACCAATCCTCTGTTGTCT  
GACCTAGGCTGAGCTCCAGGGCTGGGACCCTGACTTCTTATTACCACC  
TCAAGGTCTCTGCACTCACTTCTCTTCTGCTCAGGATTGTTTTTCTTCT  
TGTCACCAGTCTTTTCTCAGACTTAGGTCTCAGCTCAGACATTGCTGTTG  
AAAGTACTTCTACTGATCCTTTTATCTAAAGCAGCCATTCCAGCCCTACT  
CTCTTGATCATAGCACCCCTGAATTAAGTTGTTTACTTACTGTCTCTTCAG  
GAGGGCAAGGAGCTTGGTGGTGGTGTTCAGGGCTGTACCAAGCTGTACCT  
TGCTTACCCTGCTACACTTTTTAGCAACCATCTAATTTTACATGCTCCC  
TTCACCTCGTCAGAAATTTCTTATTTTCTACTTCAAGCAGGTATACATAT  
GTGCTTCTCTGGGAGGCTCACCCACTTCATGAGACTACATTTGGTCTCTG  
GGTAGAAAGTGTACAAAATCCACTGGCTCAGTTTTAATCAATGTATGTTA  
ATATTAACCAACCTGAGATCTTGATTTCCACGCCTGGCTAATTTTGTATT  
TTTAGTAAAAACAGGGTTTCTCCATGTTGGTCAGGCTGGTCTCGAACTCC  
CGACCTCAGGTGATCCGCTCACCTCGGCCTCCCAAAGTGCTGGGACTACA  
GGCATGAGCCAGCGTGCCCGGCCTAAGATCTTGATTTCTACCATCTGAAC  
TCTGTATTTGAAGTGAAGTCTCTGCTTGAAGTCTTGGCCAAAACCTTGG  
CCCCTCAGACTCAGGGAAGTTTCTGTTTCTTCCCTGGTAACTTTTCTGA  
ACTTAACCACTGGTTTGTGTTGACAAGAGATTACCATCTTCTCACTTCTTA  
GCTATGTGAACCTCACTTATCTGCTCTATTGCTGTTCACTCTAGCACGGCA

FIG. 3 (34 of 52)

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CTTATTGAACGAGTGTCTACATCTGCACCCCTACTTCTTACTCATCCAT  
TCTGTTTCAATTTCTTAAAAAGAAAAAAGCTATTGTAAACATACG  
ATTACAGAAAATGATTTATAACATGTGTATGTACCACCTAGCCCTGTCAA  
GTCTTAATATTTGTTATATTTGCTTCAAATCTTTTTTTCAGACTGTAGTTA  
AAAATTACTTAGGAGCCATTATTTATGGCCTATTTCTGACCTAGTCTTC  
TTGATGGTCAATTTGCCTAATCATCTTAAGTTGCAAAAGCTTAGAATTAA  
AGCAAAGTACCTTCGATCCTCTGCTGTTGCTTCTTTTTAATATTTGGGT  
TTGTTTGGGTCCCATTTACGGTTGTGACATCAGCTTGAGTTTGGGAGCT  
GTCTTGTTCAGAAAATGGTTCTGGGGAACAGCCTTTTCAACTTGGAGTC  
CAAAGTCTGTGCTTTTTGCTGAAAGCCATTATTGTTATGTTTATTACCAC  
TGGTTCCATTTGGTCTTATGCTAGGGGTGCTTGAATGGCTGAATTAAT  
CTGCCAAGTGTCAAATTAGGCCTCTGGCTTACGGCTTTTGACTTTTGCAG  
TACACATGATGTCTGAGGTATACAACTTGGCTGGACTTCTGATCTTGCT  
TGATGTTTGGATGTCTGTTGTTATATTCACCCTGAAGCAAAGTGGGTAT  
GTTCTGGGTTTGGTGTGCTTCACTCTCTGTTCAAGTAACAGGGTATGACCG  
TATCTTAGTTTTCAATTTGGTCTTTTCAATTTGACTCTTATTAACCTTTATAT  
CTTTGATGTTCTTGACTACTGGTTTCTTTGATGACTGAACTTTACTAAGG  
GTCCGAATAAAGTGAAGGGAACCGTCCCTGAGGGTTTTACTCCTGGTCT  
TGCAAGATCTGCTCCTCTAGAGAGTTGCTGTGATTTTACTGGGAAAGTCC  
TGCTTTGTGTTTCTCCAACAAATGTTTATTAACCTATCTTTTCAGAACA  
GCCTATTAAGTGAATTTTGCCCAAGGCTTGTGTTAGGAACTAACTGTT  
CTTGGTTTTGATTATAAGAGTCAGTCTTTGGCTTACTTCTGGTATATAATT  
TAGGATCTGGCTTCTCTCAGGTTCTGTTAAGATATCTAGCAAGTTCTCT  
TTGTTTGTCTTTTAGAAAGTTATCCAAGATTCTTTTTCAACATGGAT  
ATTATTCTATAAAGTCTATACATTTACCATTTCTTGATCTGTTAACTGCT  
GCTTTGTAGTTTTCAATTTGCTCTATATTAAGTGACCCACAGGTTTTCTT  
GACAGTCTCTGTGGTGGACTATCTAGCTTACACTGTTGAAAAGTCTT  
GCTGAAAAGCTTAGACTATGGGTTAGAAGAAACACATTTTGAAGTCCGCC  
TTTTGCCCAGAAGTTTTGGTGGCTCTAAGTTTCTGAGCTTCTGGGACCCTGCA  
GTATTAGGTGGTCTGGGCTGGAGTTTAAATGCTGATGGACCTTTTAGGTTT  
GACAGGCAAAACAACATGGTTGGTAACATCATTTTTTGGGTCTAATAGTCT  
GAAAAACAAGAAATACATATTAAGAAATCTTAACATATCTTATTGT  
TTTTAAAAATAAGTCTGTTTAAACACATGCTAAAAAAGAAATCATTTTT  
AGAATTTTCACTAAGAAAGTTGAATCCTCAGAAAGTAAAGAAAGACTCAC  
TAATAGGTAGTTTTTGTGTTTTTTTTTTTTTTTTTTTTTGTGAGACAGGATC  
TTGCTCTGTCAACCCAGTCTGGTGTGCAGTGATGCAATCTTGGCTCATTGC  
AACCTCTGCTCTCTGGGTTGAAGCAATCTCCACCCCAACCTCGCAAGT  
GGCTGGACTACAGGCGCATGTCACTACACCTGGCTACTTTTTTGTATTTT  
TAGTAAAGTTGGGGTTTACCATATTGGCCAGGTTGGTCTTGAATCCTG  
ACCTCCAGTGATCCACGCACCTTGGCCTCCCAAGTGCTGGGATAACAGG  
TATGAGCCACACACCTGTCTTAAACAGGTAGTTTTTACAAGTTGAGTTCC  
TATCAGAAGTATATTAGAATCTTTTAGCTTGACAGAATTAAGCAGAGATG  
CAGTGAATATACAAAAGTTGCTCTTTCAAAAATGAATTTGCCTCAAACAG  
TAGTTGTTGAATGCCTATTATATCCTAAGTGCCCTCCAAAGAACCCTGAA  
AAAATACATACATAATGAAGTTATGTTAGGGTACCTCCCAACAAATCTCT  
CCTAGTACTTTGTATAGCCACACTATATGTTTTTAAACCACTGCCTTTG  
TAAACATCACAGTATCACTCAAGAACCTCTGTCTCATCCCTGGAGATCAG  
TGACAAGGAGATAGGTGGCAGATGATGTGAGGCTGAGATATGCTGCCAC  
AGCTCTCAATAAACATGTAACATCTTAATAGTCATATTTGTAAAATCAGC  
CAGGACAGGGTTTTAAGGTTAGAGTCTATGTTAATAATAACAAATGTTT  
AGTCATGTGATTTAAGTTTGGATAAGAAAGGTAGGACTCGATTACAGAGA  
ATTTTGAAAAGTAGGGAAGGGAGTTTGAATTCATATGGTAAGTAATTGG  
GCAAGCCACTATGAATTTCTGAGCATCTCTCATGAAAGCAATTACTCAGA  
AAGGAGAATTTACAGAGATTTATGGAATATGTTTCCAGGGTAAGATATG  
GGAATGCTAGAGTTACCACTCTATTTTTGATTTGACAAATATTGTGAAGA  
ATCACTACATAAACTTGGCGAGTATGTAAAGGATTTCTAACCAGAACCAT  
TTGGCATTGAGGGCAAAGAAATGTCTACTCTGGATGATAGCGGTGTGTGT  
GGTGTACTAGGAGTGAACAGCGGAGTTGGGAGTGGGAGGCAGAGAGAT  
GGATGGTATACCCACAATGGCTATATCTGGATTAATCTTTGAGCACCAC  
ATTTATATACACCTCGGATCTCTCATCATTTGCTTACTGAAGAGGTGGAG

FIG. 3 (35 f 52)

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GGACGTTGGCATGAAAGCTCCAAATGTGTTTTTTAGTTGCTTTCTTA  
ATATTA AAAACGAATTGATATAATCCACAAACCATAAAATTCAACATTTT  
AGTAAGTGCACACTTCTGTGGATTTTAGTATAGCCACACTATTATACAGC  
AATCACCACCTGTCTAATTCAGAACATATTCATCACCCCTAGAAAGAGAC  
TTGGGTTTACTTGTGGCAGTCCCTCCCCA  
>Contig38  
GGTCTACATGTGCTCGCAAGATTGGATATTGAAATATCAGCAAGAAATTA  
AATGACATAGTAGTCATTATGCCTAAATTATTGTTATTTTTTGATTGAAA  
AAAGTTGAATATTTCAAATATCAAGGTAGTAGTGAGATATAATAAGAGA  
GAGTCAGTCTTAAGTATAGAATTGCTGATTCAAGTAAAGCTCTGTTCTCCA  
ACATTTGGGCCACATTGAAGAGACCATGTAGCTGCTTTCAGCCTCGGTTT  
CCTCCTTTGCAAAATGGGGATTACACTACCTGCCTCACAGAGATGTAAAC  
TTATGACATGTTATCATGATTGCCAGGGCCACCTGTTTTCTTTAAACA  
TTGAAATCACTGTGCCTGAAACAGGGATTTCCCTGCCCTTTGTGCAAGCT  
CCAGAAACAGGAGTCAGCCTGAGTCCCGCAGCTAAGAACGTGGATTCTGG  
TCATTTTCTCATAGCGAACACACTTCACAGGTCCTTCAAGGGAGTACATT  
TTCTTATAACTCACCTTAATCTCAGTTGAAGCCTCGTTTCTTATTTTGCA  
CTGTGGCCAAAACTAAATCTCATTTCTTTCACGTAAACTTCAGCAATTC  
AATAATAGTACAGTCATTTTATGTTTCAACTGAACCAAGTCAGGGTTCCA  
CTCCTGCCCTCCCCTTCTGCTCTGAGGACATCCATGAAGTGGAGGGGGTCT  
TATGTAGCCTGGAGCTATTGGTGAGGGGCGATGGGTCCGTGGTGGTCTTG  
GGGAACTGCGGGGCTGTGTCTGGCTGGTCTGGTGTCTGGTGATTGGCCTT  
GTTCCACGCGGTTACGCTGCAGGACAGTTCGTGTCTTCTTGTCTTAAT  
GATCAGCTTTTAGGCTCACGGGCTGTCTCTGCTGAGATATGGAATAGGA  
CAGCCTCTGGATCTTCTTTAAACTCTCCTGGGGCCACAGGGGACTCTGTT  
TGTGTCTGTGCCCCACATAGGATGATTCTGCCCAGACCTTTGCTGCCATTT  
CTTGTCTGTTCTGCTGTTTATGTTCTCTGGAGGGCTTCAGTTTCTTGGG  
GTCCCTGTGGAAGCAAAGCAAGTCTCTCCACGCTCAGATGTCTAAACG  
TATCTGGGTTTTATCGTCCACCCATCCCAGAGCTCAGTCTAGAGGAGGGG  
GCAGCCTTCGGGTTCTCTCCTTCTCCCAGAGCCTCTTCTTTGCACCAG  
GGCAGCCTCTTCTATCTGTTGAAAGGGCTGTCTGGTTCTTGAATATAG  
AGTTGCAGGTTTGAAGGGTGTAGGCTGAGGTAAGGCAAACTATCACATGG  
AATAAAAATTACCCTGTGTCAAGGAACAACCAGAGCTGGACAGTTTTTAA  
ATGTGAAAACCAATTTTATTCAGGACTATGGCGAGAGGTGAAGTAAGACC  
TCAGTATAGAACTGGGCTCAATTCCGAATGCAGCATGGGCAAAATGGGAAT  
GTATAGCCTAGGAGCAGGGTGGGAACCTGTGGATGAAGAATTACTAAAAG  
GGCATATCAGGGGTGAGGGGGCGTCTGGCTACACCCACTAACTACTGTT  
GCTGAAGAAAGGCTGGTGACATCACTGGGGAATGGTGGGGGATGAAGAA  
TCCAAATCAGATGGATATTGAGGATAAGGGGATCTTGATAAACTGGCTTAG  
GAGGTTTTTGTCTAAACTGGTTTTTCATAGGTAAGTCCACAGACAGGTCT  
TGGAGAAAGTTTCAGGGACCTACGGTTTTGTTCCGGGCAGATGCTTTGTCTC  
TGTCACACTGGCACTGTACCTGGCTTTCCTTTAGTCCCTCCCCCTTTT  
TTTTTTTCTGGAGTAGTTTTGGGAGACCAGAGGAGCAGGGAGTTAGGGAG  
AGTAGTCAGAAAAGGCCAGAGAAAATAAGGAGGTGTCTGTAGGGAAAATC  
CTTAAATCCTCTAATTAATTAATTTAATTTATTTATCTGGGACAAGGTC  
TCACTCTGTTGCCAGGCTGAAGTGCAGTGGTGTGATCTCGGCTCACTGC  
AGCCTCGACCTCAGGGCTCAAGCAGTTTTGCCACCTCAGCCTCCTGAGTA  
GCTGGGGCTCACAGGTGTGCACTACCATGCCCGGTAATTTTTGGGTTTTT  
TTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTGTAGAGATGAGGTTTCGCCATG  
TTGCCCAGGCTTGGTCTCGAACTCCTAAGTGATCCATCCACGTCGACCTC  
CCAAAGTGCTGAGATTACAGGCATGAGCCACTGTGCCCGGCCTAAATTCT  
CCAATTTTTAAATGCTTCCCTGTTCCCTGTTCCAGATTTGGGATATTGAC  
TGCTGTTAAATCAGCGATTTCTCCCTGTGGAGAGGTAGCCAATAGGAAGC  
AACAAGAGTGAGGAGTCTTATATCGAAATAGAGGGTAAGAGAAGAGACA  
GATGTTATCTTGGCAGTGATTAAAGAACAGCGAGTCTGTAAGCAAAGCAA  
AGCAAGGCTCCCAGGTGCTGAGAAACAATGGCTTTCTGGGGAAGCGTCTG  
TGTTCAGAACCTTAAGTTGAAACATCTCTGAAGATGTTTGCCATGAAGG  
TTTTCTTCTGAAGTTGAGTCTTTCATCACTAGGTAGGCGTGTGTTGGAGT  
CTCTATCAAACAGATCCTGTGTTTATTAGGAAGCTGTGGTTCTATAAGCC  
CCATGCTAATTTTTGCAGGTAGCAGGGTGGCCCTGGCCTGACCCGGGACA

FIG. 3 (36 of 52)

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CAGTGGCTGTCTCCCTCCCTCAGGCAGGAACTCTCTCTCTGCCACCTAGTCT  
CTGCATACCCACATTTCAAGGGAGCTTCTGGGTGGTGAGTTTACCAGACT  
ATGGTCTGAGGTAGAGTTAAGCAAAACAAAACCTAACTGCATAAAGAAAC  
AGAAAGAAAATCAGGTGTTATAAAAAACAATTTGGCATTGTGTTGTGTTT  
AGCTCCGTGTCTGATTTATTGCTTCCACAAATAGTGCCGATATGCACCAGG  
CACTGTTGTAAAACCTGAAAATATGTTTTTGGATGTGCCCAGTCTGTGAGT  
ATTAAACGATGGTTGATTTGAAATTTGCTATGATTTCATATTTCTGGGGGT  
AAGATGCAGGATTTCTTTGGGGGGCTACGATGTGGCATTCTAGAATTCT  
CAAAGAATCAACCTGGTGGGACCAGGAAGAGCTGAGCTGAGGCCTCTCT  
GCTCATGTGTACTTACTGGAGATCATGGAGACAGGTGAGCCTGAGTGCAC  
GTCTCACCAGCAAGCCACAGCAGAGGGGGAGGAGGCGGAAAGAGAGCTCTCT  
CCATTTCTGAGAAGTTAATGGTAACAATGGCATAACATACCTACTTTACAG  
TTGAAATTTGAAACCCACAGCATTAAAGTGTTCCTAATGAAATTTGGCAATT  
TGGGAGTTTTCTGAGCTGCATTGGATGTGGTTTTGTCATGCTGTTAGGATG  
AGCAAGAGATGATGGAGAACATCTTCCTTTTGGAGCTTCTCTTGGACGTG  
GGTCACTCCCCTCATGGAATTAGAAAGCTTAGACCTAGACTTGAATCTC  
ACCTTCTCAAGGTGCTCCCGGGCAAATCACTTAAGATCCATCTTCTCTC  
CTCCTGCTCCTTCTCCTCTCTGAGTTTTTTTTTTTTCTTTCCAAAATTC  
AATGACACGGTACTGGTAGAAGAAAAGGTCCAAGTCTGCTTTTACAGCT  
CCCCTCATCCCCAAATGTACTCCGACCCCAAGATGACCATGTTATCATTT  
GATTGACATCCTTCTAGTTTCAACTCATTTCTTTCATGTATATGCACGT  
ACATATACACTATTTTATTTTGCCAGGGGTACCGTTTAGCTGCATTAAT  
TTCTTATAAAATAATCTATATTTACTTATGGTTTACGTAAAACAACATAC  
ACATGTAAGTGTATAGCTTGATAAGTCTTCACTGTAAACCAAAAATAAAA  
TTGGAAGCCCCCCCCAACCCTCTGAATGGACCCCTCTTCTTGGCCAAGAGC  
ATTCCAAAGTTAACCTGAAAAAACTAGTTCAGGTCTATGATGGAAGGAAG  
GTTGGACATGCCCCAGTATACCCTTCTCCCTTTTGGAAATTCAGGAAAAGC  
TGACCAGCATTAAACATCAACACAGACCTTATGTCTGATAGGAACTTTGA  
CAATCTATTCCCTCTGAAGCTTGCTACCCGGAGGCTTCATCTACAAGATA  
AAACCTTGGTCTCCACAACCGCTTATCATAACCCAGACATTCTTTCTGT  
TGAGAATAAGTTACCTTGTAACCTGGAAGCTCCCTGCTTCAAGTTCCCTC  
ACCTTTCCAGATTGAACCAATGTAAACCTTACATGCATTGATTGATGTAT  
TATGTCTCCCTAAGATGAATAAAAGCAAGCTGTATGTTGACTGCCTTCAG  
CACAGGTTGTGAGGACCTCCTGAGGCTGGGTACGGATGCATCCTTAACC  
TTGGCAAAATAAACTGTCTAGATTGACTGAGACCTATCTCAGATACTGTT  
GGGTTCAAATATATACTTATGAACTAATACACAAATCAAGTCATAGAA  
TATTTCCATCACTCCTCATCTACCCCAAAATTCCTTATGCGTCTTTGCA  
GTCAACCTCCCAACCCCATCCCCAGGCAACTGCAGATCTACTTTTTGTCTC  
TGCACCTTCAACTGACCTTTCTGTGATTTTATATGAATGGAATCATGCG  
CTGAGCAGTCTTTTGTGTCTGGCTTCTTTTGTCTCAGCATAATGTTTTGA  
GGTTTGTCCATGTTTTTGTGTTTGTCAATGGTTAATTTCTCTCCATTGCA  
GAGTAGTTTTCTATTGTACATGTGTACCACAATTTGTATATCCATTCCAT  
TGCTGATGGACATTTGATTTGTTTCCAGATTTTGGCAATTATGAATAGAG  
CTACCATGAACACCCAGGTACAAGTCTTTGTGTGGACTTATGTTTTTATT  
TCTCTTGAATGGAACCTGTCTATCAATAAGTATATGTTTAACTTTGTAA  
GAACTGACAACAATTTATCTGCGATGGTTATGCCATTTTGTTTTTCTAC  
CAGCAATACACGAGCATTTTCAAGTTGCTCCACAACCTTTGCCAAAACCTGTT  
TTCTTTAATTTGGACATTTAAGTGGTGTACAGAGGCATCTATTGTGGTT  
CTAGTTTTCTTTGCCCTGATGACCAATGGTGTGAACATCTTTTCATGTG  
CTTTTGGACATTTACATATCCTCTTTTGTGAAGTGTCTGTTCAAATATT  
TTTGCCCATTTAAACATTTGGGGGTTTGTCTTATTATTGTGTTGGGAGA  
GTTCCATATTTATTTATTTATTTAGATGGAGTCTCACTCTGTTGCCCAGG  
CTAGAGTGAGTGGCGTGATCTTGGCTCACTGCAACCTCCACTTCTCTGGG  
TTCAAGCAATTTCTCTGCCTTAGCCTCCTGAGTAGCTGGGATTACAGGCA  
TGTGCCACCACACTGGCTAAGTTTTTGTATTTTATGATAGATGGGGTTT  
CATCATGTTGGCCAGACTGGTTCGCAATTCCTGACCTCAAGCAATCCACC  
TGCCTCGGCCCTACAAAGTGTGGGATTACAAGCATGAGCCACTGTGCCT  
GGCCCATATTTATTTTTTATTCTTTATTTTGTATACAAGTTCTTGGTCAG  
ATACAATAATACCTGGTCAGATGAGATAATGAGTTGGAAAATGCTTTGCA  
AATGGGGGAGAATAATTTAAATGTTATTTATTTAAGAGCAGAGGCC

FIG. 3 (37 f 52)

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TTCTCTTTGCGGTCACTAAAGCCGTTTGCTTCTTCTGCCTTTTATAAA  
AGCAGAGTTCGAGCTACACAGGCTGTCTGTGTTGGCTGCTATTAGTTAATC  
AGAGAGTTTTTTTTTTCTTGCCTTGTCTTCTAATTTGTGACACATAATT  
AGCCACAATATGTGTTTTTCAGTTGTGACACTGGCCTGGGAAACCAAGGGA  
TGTTTAGAGTGGATTTCCTTGATTTTGCAATAATTGTGTGTTTTCTGCA  
TCTTCTTTTAAACACAAATTCATGGAAGCAAAACATGGAAGCAAAGTACC  
CTGGACATCCCCCTTCTTTATGAAATTGATTTCTCTTAAATGTAATGTT  
TGCTTGTTCCCTTACTTTAAAGCAATTTAAGAGTTTATTGAGAAAGTGA  
GCCCTGGAAACATAGATGCATAGAGAGAAAATTCTACCACCCTCAGGTCC  
CTATTGCTCTTCTCTATAAAGTGTAGTTTCAGGGCCTTTTGAAGTTTCT  
TTTTCTGCTCTGATTGTCATGTTTGTGAGTGTGCTATTTTAAAGTATTTGG  
ATTTGGTCTGCAAATCCTATGAGAGATGGCAACAGAGTAGGGATCTCAA  
GCCTGCAGGTTGTATTAAAGTCCAGCAGGGCCTTGATTTACAACAGAGGG  
TCCTTGAAGACATTCCATATATTATGCTAGGGGAGTGGCCAAGCAAACCTT  
TAATGTGTCCCTATGGTGGGATATTTGGGGTTAATACCTGCCCTTCTCTT  
AATTTCTTTTCTTTTCTTTTCTTTTCTTTTCTTTTCTTTTCTTTTGA  
TGAGTCTTGCTTTGTCAACCANGCTGGATTGGAGTGCAGTGGTATGATC  
TCAGCTCACTGCCAACCCTCCACCTCCTGGGTTCAGCAATTCTCCTGCCTC  
AGCCTCCCAAGTAGCTGGGACTATAGGCACACACCACCATGCCTGGCTAG  
TTTTTTTTTTTTTTTTTGAACNGAATCTCGCTCTGTGCGCCAGGCGGGA  
CTGCGGACTGCAGTGGCGCAATCTCGG

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CGCTCGCATCCCTCATATCCATGAGTGTCTGTGGGGCCTGCCTCTGAAA  
TAAATCCTGCCTTTGTCTCCAGTTCACCTCCAGCCACCCATCCTGGGGCT  
GCACCTCTCTCTTCCAAGCCCTCTCCCTTTCTTCTCTGGTGTCTGCCTGT  
CATGTCAAGCATATGCATCAGTGGCAGCAGGACATTTGAAATGCAACCAG  
TACAATTGGGCGCGGTTATGCCTACCAGTTTTTCTTCTTAAACATTTTA  
TATTTATGTTTGAAGCATGCCACCTTTCTTCACTTGCCAACCTTGACAGA  
TTTATTAGTTGACAACATCCGCTGATAGCATCAGTAATAAGTTAATTGTT  
TTTGCACATGTAGCTTTAATTATTCTCATTATCATTTATAGGAGTTATTC  
TTTGTAAGGGTAACTGAGTTTTCCAAAACAAACAGAAATTTGGGGTGGG  
CCCATGGAGCGTGACTCATGAAATCAGATTCTTAGAAGGACCTCGGCAAG  
TCTCTGGGTTGCTGTTAATGAGCCTGGCTGGCTGCCAGGGGTGTGTCTGC  
CCTTTATGAGGCCACCACTGTTCAAATGCTTGCTGCAGCATTACTTGCC  
TAGGTAGTGCTTGTCTTACTGAACTGTCAGGGATCCAATTCTTTGTGGT  
CTAAGTAACAATACTCAGATTCACAAGGAATTGATTAATAAGCCAGAATG  
CCAATGTATTACATTTTTGATGAAGACCATATTTACAGTGATTGTATCTG  
CTCAAGCTCAAATTAGGATTAGAGTTCTGACAAATACATATGTGAGAAGT  
ATGAGGTTAAATACTTGAAATTTGGACTTTTCTAGAAAATCTGAATGTGA  
TTGCCATTACATACTTTCTGGGGATGATGATTCTTGTAATTTTATTTT  
AAAAGACATAGAAAATACTTAAGAATCAGATTGCTTGGCTGGGCACAG  
TGGCTCATGCCTGTAATGCCAGCACTTTGGGAGGCCAAGGTGAGTGGATT  
GCTTGAGCTCAGGAGTTGAGATCAGCCTGGGCAACATGGTGAAATCCCA  
TCTCTACCAAAAATACAAAAAACAACCAAAAAGAATAAA  
TTAGCTAGGTGTGATGGTGGTGCTTGTAGTTCCAGCTACTTGGGAGGAT  
GAGGTGGAAGAATTGCTTGAGCCCAGGAGGTGGAGGTTTCAGTGAGCTGG  
GGTTGCAACAGTGTACTCCAGCCTGGGCGATAGAGTGAGACTCCGTCTCA  
AAAAAATAAATCAGATTGCTTTATTGCTGGTTTTCTTTCTAAACTGA  
GATTGGGTCCCATCATCCCCTGGCCCCCATTGGTTAATGGTTCTCCTTT  
GTCTATTGAATAAAATACAGATGTCTGCTTTTGGCAACATGGTTGAATGT  
AGACACTGCAGGGTCTTCTGACTCAAAATGAGTAAGGCTTAGATAAAAC  
ACATTTTGAATGCATTTCTGGATGAACAGCAAGGAAAGGAGATCTCTTA  
AAATCCTCTTCTGTTCCCTCTCCCTACCCCTCCAAGTGGGCTTAAGT  
AGGAAGGGTGGTGAGCGGCAGGTAAACACACGTCAAAGGCAGTCTTCTC  
TCTGAGGGAAAACACTTGTATAAGCATTGCAATCAATGGGCCTCTTAAAT  
TATGTGCCAGTGGCAAGAGCGGGTGCTGAACCCAGGGGCCTGCCTCAATC  
CGGGGGCTTTGAGGCAGAATAAAGTGGTCTCAGGTTGTTGGCATTCTCTT  
GCCCTTCCACCCGAAGCAGACACAAATCCTCTCTGGAGGCAAGTTCCCA  
ATTCAGCCAGTACAACCTCCACAGACTAAGATCAATCATGTACAAGCTCA  
CAGACAAAGGTCAACAAACACACAGAGCAATAAACAATTCATGAGTGAC



GTGAATGAGAATAAACACAAACAATAACCACCAGCTGGGATGCTCTAAG.  
CTTCAGCTGTTAGAATTCTCTGAATATAGAATAAACTGCCACAATGGCAA  
ACATGCATCTAGTACTTACTGTGTGCTGGGTTCTAAGAATTTTGCACATT  
GTGCCAGATACCGACTCAGCTTCACACTCACCTCTCTACTGTGCCCTCTT  
AATTTGCACTAGATTAAGGTTAGAAAGGAAGAGGCAGCTATTCTGTTCT  
TGGCTGTGCTCTGGCAGCACATGCAAAATGGGCAGTAACAGTGGCAGTC  
ACAGGTAAGTAGCCTTCTCACAGTGTGGAGTTAAAGGCATGGGACTGAGA  
CGAGCAAGGTTCTTAAAGGGACAGTGGCCAGTAGATGACCAGGGGCTACT  
GGAGTGGCTGCATGGCTCTGTGGAAGCTCAGAGGAGCCTTGGGTCTTGCA  
GGTGCAGTAGCAGCTTTCTGTAGTTCTGTATCTCTGGGTCCCACAATCTT  
CCCCGTTTTTGCTCTCCACTTCTAATTTTGTAACTGACTTCCCTGTGTG  
TACTTCTCTCTCTGATTGAAATAGCCAGACTGGTTTCTGTTTCTTGATAA  
GACATTGTCTGGTACGAACACAGTAACCTCATTTAATCCGATATCTCTATG  
AAGGAGGTACAATAATTATTCCTATTTTACAGATGAGGAAACACAGCAGA  
GAAATAAAGTCAATTGTCTAAGGTTGCACATTTAGTCAAGGGAAGGGTTG  
ATATAACATATAATTATTTAGAAAACATCTAAGGAAATAAAAGGCATAAT  
TTAAAAATAAAACTAGGCAGGTTTAAAAAAATGAAGTAATCTATAAGTAA  
AAAAGTATAATTGTTGAAATACATATCTTAGTGGATGGGTTAAATAGCTG  
AAGAAATGATTAATGAACTGGAAGGTAGTTCTGAGGAAATCAGAATTCAG  
CATAGATAGAAAAATGGGAATTTACAAAAGTACACAGGAATTATAAAG  
AGGTTAAATTATAGGGAGGGTAGAATGAGAATTAACATTGGTCTAACTGG  
AATTTTGAAGAAGAGAATAGAGAGAATGAACAAGGCAATATTTAAAGAG  
GTGGCTGAGAATTTTTCAGAACCAACACAACTATGACTTTACCAGTAGA  
GAAAACAATGTACACTGAGGAGGATAAATAAATATACTATGAACAAATTG  
TAATAATAATACTCAACAAAGACAAAGAGAAGATGTTAAATCAGCAAAA  
AAAGAAAGTCAGACTTAGAAAGAAATGACAATGGCAGACTACTCAACAAC  
AACAATGGAATCCAAATTCGGTCAAACAGTATTTCTTCATGCTAGCATA  
TAGC

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GGGAGTCCGCTATGCTCCTAAAGATTGTCACCTCTGATCTGGTTTGTAGT  
TAGTCTCTTTTATTGCTTTATCCTACTCAACTAATTTTTTTAGTGCCTGT  
TTTTTTTTTTTTTAATGTGTGTTGATGACTACAATTTCTAACTCATTCTA  
CTGATTCTGCGGTGCTTTAAATCTGAGCAGTCTTTCGCATTTACTGCCT  
GTGATGGCCCATCCACCAGCTAAAGTGTGTGGCCACTGCTTACAGCACC  
ATGTGATAACGAGTAAGGGAGAGATGCCGCCAGACTCTTCTAGGAGCAG  
CCAGTAGGACCTTCCAGGGGTTGCAAGCAAACACAGCAATATGTGGAGT  
GTGGCAGAGGATGGCCCCAAGAGGATGTGGCAGCGGCTAGTGCAGCTCAG  
CTTAGTCTGAGAGGAAATGCTGGAGAGGAGAGCCAGTCTGTACAGGCAT  
GACAGCCACAAGGACTTCAACAGCTAACATGGCTGAGTGGACTTTATGTG  
CTATCTCATTTCAGAAAACAGGAGCAATCAGAAAGGAGTCACCTCCTATTT  
GTACCCAGGAATTGCTAACCTACTTGCATCTGAATGATGTCCATCACTT  
CCCTTCATCACCTCCTCTGGGGGCTCTGCAAGGATTTGACTCCTGCATTA  
GTGATCTGTCTCACCTACGTTGTGATTACATGAACTTACTAATGTGCTA  
TGTGACAACTACCATCTTAAACACAAAAACCTCTTTTGATTCTGTGGCT  
CCCTCCAGCTACCCCTGCATTTCTGTGCCCTGCCCGTCTCTGCACT  
CACTTTTATTTTACAGCAAACTACTCAAGGGAGTCTCAGTGTCTCCTTGG  
CTCCATGTCTCCACCTTTTATTCTCTCTCAGTTCACCTCTGTGAGGCTT  
CCGTCTCAAGCTCTTCTTCACTTTTGTCTAGGGCCGCTGACATCCTCT  
TTCTTGCCAAATTGAGTGGCCAGGTCCTCACTTACTCAACTGCTCAGCAT  
TGTTGGGCTGGTGGACCACTTCTCCTTCAACCCACCTTTTGCTGCTCTC  
TCTTCTCTCCAGATGTTTCTCTCTCTCACTGGCTACTCCTCTTTTGTCT  
CCTTTGTTAGCTCCATTTCTTCTTCCAACTCACTGTGCTGGTGTGCCC  
AGTGCTCAGTTTTTAGCTATTCTCTCTTTTCCAGTGGCATTCTAGATG  
GTATCATGTGACCCATGGCATTATATGCCTTCTACATGACAGTTACTCCT  
GAATATGAATCTCAGGAAAGATTTGGATTTATTTTAAATTAATTTTTTTA  
AATTTTATTTTAAATAAATGAGGTCTCTCTCTGTCTATCCAGGCTGGAGTGT  
AGTATTGAGTGTGATTATAGCTCACTGCAGCCTTGAACCATGGGCTC  
AAGTGATCCTCTGCTCAGCTTCTGAGTAGCTGGGACTACAGGCATGT  
GCCACCATGCTGGAGTACTTTTGTGTGTGTGTGTGTGTGTGGAGACAG  
GGTCTTCTCTATTGCCAGGCTGATCACAACCTCTGGCCTCAAGTGAT

FIG. 3 (39 of 52)

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CCTCTCACCTCAGCCTLCAAAGTGCTGGGATTACAGGTGTGAGACCAJ  
CTGGGCTAAGATTGAGATTTGTATTCAATTGACTGTTTGACATCTTCAC  
TTGGACACCTAAGAGGTATCTCAAATATTAATTAACCTGGCCAAAATACA  
GAACCTTTTGACCCCTGCCCCACAATACTTGCCCTTTCCCCAGACTTCTC  
CATTTCTGTAAATATCCCCAGTTACTCAACCCCTCAAACCTATGAATGCC  
CTTTGATTTCTTTCTTTCCCTCATCTCCTACGTTGACGCCATCAGCTAGT  
TTTGTTCCTTTATGCCAGAATATAATCCTCACCACCTTCTCTCTTATT  
GCCCCAGTATAAGATGTCAGTTTTTCTGCACAGTCCATTGCCCTGACCT  
CCTGAGTGGTTTGTCTCCACTTTTGACATTTGTATTCCTCTTTCCCCCAG  
GGTCAATTTTTCACAGCAAGAGTGGCATTTTTTTTTTTTTTTTTTTTG  
AGACGGAGTCTCGCTCTGTGCCCCAGGCCGGACTGCGGACTGCAGTGGCG  
CAATCTCGGCTCACTGCAAGCTCCGCTCCCGGGTTCACGCCATTCTCCT  
GCCTCAGCCTCCCGAGTAGCTGGGAATACAGGCGCCCGCCACCGCGCCCC  
GCTAATTTTTTGTATTTTAGTAGAGACGGGGTTTACCTTGTTAGCCAG  
GATGGTCTCGATCTCCTGACCTCATGATCCACCCGCTCGGCCTCCCAA  
GTGCTGGATTACAGGCGTGAGCCACCGCGCCCGCCAAGAGTGGCATTT  
TTAAAACCATATATTAGATCATTGCTTTTGTGTTTGGGAACCTCCAAGGG  
CTTTGCATCATATATCAAGTTGACACCTCTCCTACCCAAGCCTGGCTCTT  
TCCTGCTCCTCTGTCTCTCAGCCCCCTCCACCCATTGTTTATGCTGCTTC  
AGCCACACTGGCCTTCTTGCCATGCCACATTTGTGCTAAGCCCACATCCA  
ATCTCGGGGCTTTGCACTCGCATTTCTCTGCTTGGCATGCTGTACCCC  
AGATCTTTTCAATGATTGGCAGCTTCTGTACATTGAGCCACCTGCTCAAGCC  
ACCTTTTTCAGAGGGCTTCCCTGGCCACCTCACCTGAAATAGCACCTCCG  
ATTGCACCCATCCGGTTATTCTCCATCCTGTTCTCTTCTGCTGGTGATTTT  
CCATCACTGATGAGGAAATGAACCATGGAATGCTAGGGCTGATGACCAGA  
ACTTTCCCCCACCACCATATTACAGAGGAGGAAATGAGGTGCGAGGT  
AAGATGGGCCCAGGATTTCTACTCCCGCTGGACTGCAGGCACAGCACTG  
ACCTCAGCTGTGCTCACTCTTGCCATTACCCCAACCTTCTATCTCCAAC  
TGCCCCATTACCAGAAAGTGAAATGTTCTCAGAGACGGTGAGCCACCTG  
ACTTGGACAGCAGGGCCCTGGCCACCTGCTTTCTTCTCCTCCCTGC  
CATCCTTTCTCTCCAAGACCTACCTTTCCCTGTGATTCTTGCCACATG  
CTGCATTTTATGGTTTTATGACCTGATTTCTGAGAGGGATTTGAATTTTC  
ATGATTATTTATGTAAGCAAATCATTATGCTTATACAAATGAGAAAAGGA  
GTGCTTCTGGACTTCCAGGGACAAAATCTTGTCACTTGGCTTGTCTTCA  
TATTGCTAATTAAGGACCCAGGATGTGGGTGAGATGTGCTAAAAGCTGAG  
AGGAGGCTCTGGACTCTGACTATGGGCCCCACACCCCTGGGCAGGCATCAC  
ACTAGTCCTTTAGGTCATCTTCAACCCAGCTTCCAGTTGAATCAGATGTT  
TGTGAATAACTCAGCAAGGCTGTATGGGAAATGAAGAATGAGGTGGGGAA  
GAGGCCTGTGAGAAGACACACTGACTTACCCCTCTACCTCTAACTAGGG  
TGTGTAGCAGCCACCCACCCACCAAGTCTGTCTTCCAGACCACGTATGC  
TTTCTCTCACCTTTGCATCTTTTATCTTCTGCCAGCCCAGATGCTTGCTG  
ACTCCAGCCCCAAGCCTATAGGATAAGCTACAGCCTGTCCCTACAGACTAC  
GCATTGCAGAATCTAAGACATCAAGTCAAGTTCGGAAGCACTTGCTTCT  
CCTCTCCAGGTACACAGGCTCTCCTGGAAAGCTGGTAGCAGCTGTGGAGG  
TGTGGTGTGTTACCTGCTGCAGGTGCAGAGAAGTTGACTTCACAGCCCTT  
CAGAAAGACTGCCTTCTTCCAGTTGTATTTGTGTACTTGCTTGGGTGTGG  
GGAGGATTCTCAGCTTTCTCCACTCAAATTATCAGACCCCTTCCATTAG  
TGGTAGACCATTTCCCTCGTCCAGGCCAAGGGCACATAGTACAGAGAAAT  
AGGGAGTTGTTACCCAGGGAGAGAACTTGCTCTAAACCTGTAATAGAAA  
GGTCAGTCTGGTCTGGAGGGTCAATTTTGATCTTTGGCTCAGATCCAGG  
AATTGGAACCAAGGCTTTTGAACATTTTAATGCAGGGGATTAATAAATG  
ATACGAGTCAATCAGGAATATATTTGCTTAACATCTAAAGAGATCCCTCA  
AAACACTAGAAAAAATAAGAACAAAAATCTAATAAAACAAAAATTTGTAA  
ACACATTTACCAAATTTTTTTTTTTTGGTAAAAATTCAAATGTCATAAATA  
AAGCTAAAGTTCTCTTGATGACTCGCTCCTCTGCCCTATTCCACTCCAA  
GTAACCACTATTATCAGTCTTGCCAATACCTTCCAGACCTCTCTACCTC  
TATATACCATTAGAAGCACATGGTTTTGCATTGAGGATGTGCAGTGT  
GTTTACAGTAAATGTTTATCACTCTGTTCTTGTTCATAAATTTGCCTTTT  
CTCTCAATGATTTGCTTGGCTATCTTCTATTTCAGTAGCATCTCCTTCT  
TTTTTAACCTTACCATTGTTTATTTAACCTTGCTCTATCAACAGATATGT

FIG. 3 (40 f 52)

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AGGTTCTTTCTAGTTGA. TTCATTAAGTATTTATAAACAACGCATCAG1A  
GATGTCCATAAAATTTCTTTACGGAAGATGGCAAGTAGTGGAATTGCTGAG  
CCAAAGAACATGTTTAAAAAACCCAAAAAACTAGACGCTACCAATTTTC  
TCTCCAAAATGGCCATACCCACTTACCCATACAGAGATGATTTGGAATCT  
GGCTTCTCTACAAGGTGAGATGCCTTCACAGTTTCATTCTTCTGGCATG  
TCTTCCCTTTTGTATCTGAGAGAGCTGGCAGAATTGTGTCACTAAATCAA  
GGATAGAGGGTCAAATGACAGCTCAAGCTCACAGGCACCTCTGCTTTCTT  
CCCAGACCACCTGCTTTCTGCCACCAGCTCTGTTCATCTTATAGAATG  
GTTGCCACTTGGGTGTCTGCTCCGACAGCCATGTATCCTTTGCACTGCA  
GTTATGAAGCAGACAGAGCTAGGAGAGGGGCTTTGCCAGCCTCTGCCCTA  
GCTTGGAGAATTTCAAAGAAGGAGGGTATTGAGAGTGAGCTGCCGAAGAC  
TGGCAGCTCCCTCAACTCAACAGTTGTCTTCCACAAGAAGTCAGATACA  
TTTTTTTGGGATAAAATATTTAAAAATTATTATTTATTTCTGAATAATA  
TATTTACATGTTCAAATCAAACTGTAGGCCAGGCATGGCTGCTTATG  
CCTGTAATCCTAGCAATTTAGGAGGCCGAGGCGGGAGGATCACTTCAGCC  
CAGGAGTTCAAGACCAGCCTGGGTAACATAGTGAGACCCTGTATCTACAA  
AAATTTAAAAACAAAAATTAGTTGGGCATGGTGGCTGATATGGTTTGGCT  
CTGTGACCCAACTCAAACCTCATGTTGAATTTTAACTCCTCAATGTTGAGG  
GAGGGTCTGCTGGTGGGAGGTGATTGGATCATGGGGTGGGTTCTCCCTTGC  
TGTTCTCATGATAGTGAGTGAGTTCTCACAAGACCTGGTTATTTGAAAGT  
GTGTAGACCTCTCCCTTCACTCTCTCACTCTCTGCTCCGCCATAGTAA  
GATGTGTGTGTTTCCCTTTTGGCTTCCGCCATGATTGTAAGTTTCTCTGAA  
GCCTCCAGCTATGCTTCTCTGTACAGCCTGTAGAAGTGTGAATCAGTTAG  
ACCTCTTTTCTTCATAAATTACCCAGTCTCAGGTCACTCTTTATAGCAGT  
GTGAGAGTGGATGAATATAGTGCCATATGTTTGTATTCCAGCTACCCAG  
GAGGCTGAGGTAAGAGGATTGCTTGAGCCTGGGAGTTTAAGGCTGCAGTG  
AGCCATGACTGTACCCTGCTCTCCAGCCTGGGTGACAGCGAGACCTTGT  
CTCCAAAAAAGGATTAATTTGGCTCACAGCTTCGAGGCTGTTCCACAGGAAG  
CATGGCAGCATCTGCTTCTGGGGAGGCCTTAGGAAGCTTTTACTCATGCA  
GAAGACAAAGCGGGAGTGGATGTCTTATATGGCAGGAGCAGGACTGAGAG  
AGAGAGAGAGAGAGAGAAAGGATGCCACATACTTTTAAACAACCAGATCT  
TGTGGGAAGCTCTGTACAGAGAACAGCACAAAGGGATAGTGCTAAACCAT  
TCATAAGAACTCCACCCCATGATCCAATCACCCACACCCAGGCCCCACC  
TCCAACATCGGGGATTACAATTTGACATGAGATTTGGGCTGGGACACAGA  
ACCAAAACAATACCAGAGTGCTTTCTCATTCTTTCTATAGCTGCCTAGTA  
TTCTATGTCTTTTACTTCAATTTAGGCAGTCTCTTGTGATAGACACTTGG  
GTTACTTCCAATTTTTCTTATTACAAATGATGTGCAATGAATAATTTTGA  
TCATTTTCCATTTTACATGGGTATGTCCATCTGTGGGATAAATCTCCAG  
GAGTGAAATTTGCTGGATCAAAGGGGAAGTGCACTTGTGATTTTCAAGTT  
AGCAAAATTTGTTCTATAAGGGTCATATCAATTTATAGTCCACGCGTAA  
TATTTAACAGTGGGGATTTCCCGACAGTTTGACCAACAAGGTCTGTTGTT  
AAACTTTTGATTTTTGTCAATCTGATGGGAAAATACTAGTATCTCAAAGT  
GCTTTTAATTTGACTTTCTTATTACAATGTTAAGCATCATTTTACTCTGC  
CCAAGATCAAATAGTATTTTCTTTTCTGTGAACAGACTGTTAAGATCCCT  
TGCCTCTTGTGTTTGTGCTGGATTTTTGTTCTTTTTTTCAAATGTTTTGAGG  
CAGTTCTTTACATGTGAAACAAGTTATCTCTTTATCTGGGGTGTGAGTTA  
CAACTACTTTTCTCTGGCTTGTGTTTGGCCTTTGACTTTGCTTCTGGTGA  
TTCCCGCAATCTGAAAGTGACTTTTTGTCATCATTCTTATACACC  
CATGCTCTTGTGTTTCAAGCTGGTTCTCTACCTGAGGGCTTTTCTTTTCTG  
CTTCTATCTGGGAACATTTTTTTGAGAGAGAGTCTCACTCTCTCGCCAG  
GCTGGAGTAGTGCAATGGCGCGATCTTAGCTCACTGCAACCTCCACCTCC  
TGGGTTCAAGCAATTTCTCTGCTCAGCCTCCCAAGTAGCTGGGATTACA  
GGAGCCCACCACCAAGCCCAGCTAATTTGTTGATTTATTTATTTATTTTT

FIG. 3 (41 of 52)

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TGTAGAGATGGGAGTC. LACTATGTTGCCAGGCTGGTCTTGAAGTCC. J  
 GGCTCAAGCGATCCACCCACCTCGGCCACCCAAAGTGCTGGGATTACAGG  
 CTAAGCCACCATGCCCAGCCCATGTGTGGAAATCTTCTGTTTATCCCTT  
 TAGGCTTGATTCTTATGTCTGTTCTCCTCCCTCCTTCTGGATACTCCTCT  
 TGTCTTTATCTTACTCTACTTGTCTATGTTACCTTGTCTTCTGCTTATAAC  
 TAGCTCCCTCTCCTATCTGAGGAGGGACTTGTGACTGTTCTCATCTCTGT  
 ACTCCAGCTCCTAGTACATAGCGCTTGCTCAACAGATGTTTGGTGCATT  
 GATAGATAAATCACTGGTAGCTGTACTACCACTCCTGACTCCCTGCAGT  
 GCTTCAGCTGATCCTGTTCCAGATGTGCACTGAATATCCTTCTGTTGAAC  
 AACAGAAATAAAGGGGATGGGTGAGGAGGATAGTCTTCGGTGGCCAAGGA  
 TATTTTAGGTACTTTGACCACTCAGCAATGAGGAGTGGGCTTTAGTCC  
 CCAAGAACTCTCACAGCCCTGGGTGTCTTACTGTTCACTGTCAAATCC  
 AAGACAAGTCAATGATCAGGAAAGACCATTTTTTTTTGTTCAGTGAAGTT  
 TATTTGAGAATCATTGAACAGTATGATATTTGGTAATTTATAAATATTC  
 CCACCTAAAATGATCGGAGCAGATATATTTTCACTCGTAATTAAGGACA  
 TGATTTAAAGAGAGCACACCAGTCCAAATTGAAATGATTCCATAGCTATT  
 AAAAACTAGGGTTTTTACAGACAATGATACTTTTGCCCCCTTTGAAT  
 AGATTAGACCAATGAATAAAACAAACAAATAAATAAATAAATAGGG  
 AAGCGGTTGCTCATCAGAATGTGGGAGCGAATGACAGAGGGTTTCTTAGA  
 ACCAAATGTGGCCGTGGTTTCTGTGAGGCGTGCTTAAAGTGAGTAGGAGA  
 GGTGAGAGAGGCTGGCTCAACAAAAGGGCTGGGGATTGTCCCTGAAGAA  
 CCAGAGCTGANTTNCATCAGGAGTAACANAGGTAGATAG

>Cont:1341

CCGCGTTGAGGTTCCACGCAGTTCAAATTATGTCCAATTATCAACATTAA  
 TGCACATTTTCAATAGAACCTGTTCCGGCTTTTCTTAGGAGGGGGCGGG  
 GAGACGTTGTTCTCTGGGAATAAGTGTACGCAGGAGGCTGAGAAGGCTTC  
 ATTCCATAGCATTCACTTACCTCCAGCTGTAGAGTGGGCTTATCATCTTT  
 CAACACGCAGGACAGGTACAGATTTTTTTCTTTGAGGCCCAAGGCCACAG  
 GTATTTTGTCACTTCTTCTCTCCTTGTACAAAGGACATGGAGAACACC  
 ACTGAAGAAAGAAGGGGGTCTTGTGGTTAGGGACACAGCAGTGCAGGGTC  
 ACCCCAACCCCTAGGCCCATGAGTAGGATACATGTAATTTGGTAGCCTC  
 TGTGGGAACCCACAGTGAAGTTCCTTGGCCTAAGACACAGGATAACTTGA  
 CTTCTCACAGACAATAGCAGGGTCATTTTGTTGATTTAGGGTTTCCCTC  
 AAAGGCCTGAGGGTTTCTCAGAGCCTCATAGCAGTAGGAACGGAGAATGA  
 AAGAGGGTCTACATTTTAAATGCTGAAGGAAGGAAGGAAGGAAGCCATTG  
 TGTCACTGGCTGGCAATGTGCCCATCCACAGGAGCGGAACAACTTGATCA  
 ATGTGGAAGGAAGGAAGAGGTGAGGCTGTACTTCTGCCAGAAATCAGG  
 CACCAGAACTGTTTTCAGGAACAGAGAGTAGCCCATGGGAAGAACTGGGA  
 BAGGAGAGGCTGAGCTGGGAAGTGGCTCCAAAGAGAGACACTCATTTTG  
 ATCTTCTCAGTCAAGCAGTGTCAATTGGAGGCCCTGGGATCACTCTTA  
 CTACCCGATTCCAAAGAAACAGGATTTTCTTGGCCTGGCTGAGAGCAAAT  
 AGCTTCCCCCTGAGTGAAGGCTGTCTTCAAAGTCAGCAGCCTTAGTTGCC  
 CACACTCCTGTGCAGAGGCTTTGGCTACTGTGGCACGATGCCAGGCAGAT  
 CACCACAGCTAATGATGGGTTACCGCACTTGAAACTTTTGCCCGTTACA  
 GCGGAGAGATATAAGTTCTGTGGGCGGTAAAATTTCCCTACAAGGAAC  
 CACCTGGCAATTGGGTGGGACGGATGTTGGGCAAGGGGGGAAGACTGGGG  
 AGGGGGATGGACACATTATCGCTCCAGCACTCTTGTTCAGCCTCAACAA  
 CAGGAAGAGAGAACCACAGGCAGTTAGGCCATGTCCATCAAATGACCCC  
 ATATTGTGGAAGAATTGACATTGCACTATGCCCAAGAGACTTGGGTGGAC  
 ATGGTCCTGGGAGTGCTTGAAGCGTCTAATTTCTCAGGGTCACACTCCTG  
 TTAACAAATGCACTGGCCAGTGCAATCAAATGTGCCATTTCTAGGACCAA  
 AGTTTGTATATCTTTTAAATATTTTTTCACTTGTGTTGATCATTTG  
 CTTAAATTAACCTTCTACTTTGTTTAAACATGGAGAATTAGCAAGCTG  
 CCAGGAGGCCAGGCAGGGAACAGGATGTTTCCATTTACCTTGTGCTC  
 CATATCCTGTCCCTGGAGGTGGAGAGCTTTCAGTTCATATGGACCAGACA  
 TCACCAAGCTTTTTTGTGTGAGTCCCGGAGCGTGCACTTCAGTGATCGT  
 ACAGGTGCATCGTGCACATAAGCTTCGTTATCCCATGTGTGCAAGAAGAT  
 AGGTTCTGAAATGTGGAGCACATGTTGTTTAGGTATAAATCAGAAGGGC  
 AGGCCTCTGAGGCGAGGTGGCAAAATTTGATTCTTGGAGGACACCTGA  
 GCATATACGGTCAAAGTCTGATGACAACACCAGTAGGGATGAAGCTGGGA

FIG. 3 (42 of 52)

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GTGGGGTGGCTAAGAALCTGGACCTGACACTATTAGACATGGGTTCC...  
 CTTTCAGGTCTATTACTGCTCACTGTGGCCGAGCAACAGAGCTACTTAGGT  
 AAAATGGTGATGGTCATAACACTAGCCCCACAGGGAGGTTACGAACCTCTG  
 GTGACAATGTAAGTGAAAGGCCCTTGAGAAAGAGTGAGGGAGTTGCAAAT  
 GTCAGTAGCCATCAAGATCTTCTTTAAGAATAGTTTCCACTAAAGAGATG  
 ATTGCTTTGGTTTCCAGCCTTCTTTGTTTTGTCTCCCCGCTGGGCCTTCT  
 ACCTTTAAAGGGCTTTGGCTCTGGGGGAATTGAGTTGGCTGGGGCTTGAT  
 GACTTCCAAGAGGACACAAGTGGAGATCTACTGCCTGCTCTTGGCTAACT  
 ACCTTCTTCAAAGATGAAGGGAAAGAAGGTGCTCAGGTCATTCTCCTGGA  
 AGGTCTGTGGGGCAGGGAACCAGCATCTTCTCAGCTTGTCCATGGCCACA  
 ACAACTGACGCGGCCTGCCTGAAGCCCTTGCTGTAGTGGTGGTGGGAGAT  
 TCGTAGCTCGATGCCGCCATCCAGAGGGCAGAGGTCCAGGTCTTGGGAAGG  
 AGCACTGCGGAGAGAGCGAGGGAGGGAGCCTGGTGAGGTGGTCTTGCCAG  
 GAACCATGCTTTGACATCAGAGAGTAGAAAGCTCAGAGAGGAGGAAAGGG  
 CTTGAAAGAATCCCGAGCTTCTAAAGATCATCCCTCTCTGGGCCAGGCGT  
 GGTGGCTCATGCGCTGTAATCCCAGCACTTTGGGAAGCCGAGGTGGATGAA  
 TCATTTAGGTGAGGACTTCAAACCAGCCTGGCCAACATGGCGAAACCCC  
 TTCTCTACTAAAAATACAAAAATTAGCTGGGTGTGGTGGGGTGACCTGT  
 AATCCTAGCTATTGAGGAGACTGAGGAAGGAGAATCGCTTGAAGTCAAGGA  
 GGTGGAGGATGACAGTAAGCCAAGATTGTACCACTGCCTCCAGCCTGGGC  
 AACAGAGTGAGACTCTGTCTCATAAAACAAAACAAAACAAAACAA  
 AATAAAATAAAATAAAATAAAAGATTATCCCTCTCTGAAGCTCAAGGAG  
 GTTAAGGGTGTACTCAAGGGCACACAGCAGGTTAGAGGCAGACTCAAGAT  
 TAGAATGTGGCCTTTCTGACACCTTACAGGCTATTCTTTTAGAATAAATC  
 CCATTTCTACTTTGTTTCTTTTGTACATGCCCCACCTACACCATAC  
 ATGTATACCTTCTCTATATCTTTTGTATCCCTAATGCTGTCAACTATG  
 ATTTGCTTTTTCATGCAGATGACCATAACATTTTCCATTACCTATGCTC  
 ACTCAGCAAGTATTCAATTTTTCTACACTGTTCTTTTTTTCTTTTTCA  
 TAACACTGTCTCATAGGCATTCTGCAAATCCTGTGAGAGTACTTTTGTG  
 AAATGTTACCACTTTCTCTTATTGAGAGAAGCTCCGTATTAAGGCTTCA  
 CTGAGGTGGCCTTAAAGGCATGATAATGGTTCAAAGGCTTGAAAGACAGTT  
 AAAGAGACCTGTAAGTGACAAAAGAAAGTTGAGCAGGAGAGAATTTCT  
 GCCTGGAGCAGAGCCAAGCTGCTGGAAGAGGCAATGGGGGCAAAGGCCAG  
 GCAGACAAGCCAATGGGCTCCTCCACAGCTGCAGCCAACAAGTTATGCC  
 AGTCTTAAACTTCTAAAGAAATATGTTTTTAACAAGATTGAGGACTGGA  
 TTATGAGGCTAGGGGAGGCTATCACAACTGGAATAAAATAAAGCCAGAG  
 AAAAGTGGCTTCCCTTCAACCTGCACAACTGACCTAGCTAGGCTGATGGC  
 TGGGGCACCTGAGGAGGCTACTGAGCATCATATAAAACAGAAGGGACAGC  
 AGGAATATAACATGGCTCTTTGTAAGGATGAGTCTGAAAAATGACCATT  
 GCTGCCCCAAATGCCCTTAGCTACAACCTGAAAATATTTGAACTGGAGGT  
 TGCAGGATGCTGGAATCTCAGAGATCATCCAGCTCAGCCCTTTATTTTC  
 AGATGAGGTCCAAAGCGGGTAAATGACTTGTCAAGGTCAAACAGCAAGT  
 GAATGGTTTTCTTCAAGTCTCAATTATCTTTTTGTTTATATCATCTAT  
 GCTTTGTTGTTATAAGCTTCAACCCAGGTAGCAAAAACTATTCTACTCA  
 AAAGGGGTAGACATATGTTAGTTCTCAAGATCATCTTTGTTTTCAGAGT  
 TTAACCTCAAGTGATTGGCATAGGCTGAATCCATCTCTTAAAGGATAATC  
 AAATTTATGTTGAAGACTTGGTTGTCTTCTACTATGAAATGGGAAACAT  
 TATCACTACTCCTCCCTGTCAACCAAGTGTGGCCACCACCACCAACG  
 TTAGTGAGTGACTGTGGTGATATGATGACCAAGTGGCCAGGTGAGCAAGT  
 GGTGCAGCCTGTGTCTCACTGGAAGAGGTTAAAGTCTTTCTAAAAACAAA  
 TACCATGGCATCAAAGTGGCCCAAGAACTCCCTTCTTTGAGCTTTCCCTGT  
 GTTAGAGCCCTTCTTGGGTTGGGAGTTAAACCCATAGTCTTACCTTCAT  
 CTGTTTAGGGCCATCAGCTTCAAAGAACAAGTCATCCTCATTGCCACTGT  
 AATAAAAAACAGGGACATGTCTCAATTATGTCTTCTAAACAGGTTTATTTT  
 TCCTTCCCTGTGTACAAGACTTGACTGTTTATAAGAACTGCAACAGCC  
 TGCCTCTCAAAGCTGCCTGAAACACCTGGCAAGTTTACAGTGATATGCG  
 CAGAACAGTCCAGAAGGCAGATTCTAGGCCTGGCAGGTGGGCACCCTGGG  
 TGCTCCCTGTTGGATCTTGAGGCCTAACCTCTAGCCCAAGAGTCAGCT  
 AAAATCTAGGCTTCTCCCTCTCCCTCCAAGCCACACTTTGCAAAGGGATT  
 CTTGTATTGTGGGCTTGAATCTTTTCTCCCATTTGCTCTGCAGGAAG

FIG. 3 (43 of 52)

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CCCTTGCAACAACACA TGGATAGCCTCCAGGTCCCAAGGCTGGAGC  
CTTGTAATGGGAAAGTAGTCTTTAAATCAGATTTACTTGGCACCCCTGTTT  
GCCACTGAAAGAGGCAATTTAGGGGAAAAATCTGGTCTCCAAGCACAGAT  
AACACTCTACTCTTGAAAGAGGAGACCTGCTCATGTTACTGGTCTCAGCG  
TCTCCACTGACCTGTAATAAGCCATCATTTCACTGGCGAGCTCAGGTACT  
TCTGCCATGGCTGCTTCAGACACCTGTGTAAAAAGGAGAAAAATGAGTGAC  
TTCCCATGACGGCTACGTTTCATGTGTGATTTCTCTCAGCATCEAGTGCA  
TGGCAGTCATGCAAAGAAATGATCTCTGAGTAAATGAATGAATGTGTGAA  
AGAGAAGTCCCTTGGGTCTAGAGAAAAGCATTGCTAAACCAAACCCCAA  
CTAGCAATGTATTGGCTAGGAGAGCTGGAGCAGAGGCTTTGACACTAACC  
TTTAGGGTGTCTAGCTGTTAGATAAGCAGTATCCATTCCCAGAATATTTCC  
CGAGTCATAAGCATTATATTACACCTGGCATTTTTGCAAAAAGCTGAGAG  
AGGGAGGCAGAGAGGGAAGGAGAGGGAGAGACAGAGAAAAGAGAGAGAG  
AGAGAGAGAATATGCATACACACAAGAGGCAGAGAGACAGAGAGACTCC  
CTTAGCACCTAGTTGTAAGGAAGATTAAAGTCATACTTGAGCAATGAAGA  
TTGGCTGAAGAGAATCCCAGAGCAGCCTGTTGTGCCTTGTGCCTCGAAGA  
GGTTTGGTATCTGCCAGTTTCTCCCTCGCTGTTTTTATAGCTTTCAAAAG  
CAGAAGTAGGAGGCTGAGAAATTTCTCTGTTGAATACCTGATTTACAAT  
CAAGTTAAAGGAAAGGGGAAAGAGTATTGGTGGAAAGCTTTAGGGGAG  
GGGACTAATAAACTGAGATAATTCTCTGGTTTCATGGAAGGGCAAGGAGTA  
GCAAACATGACACATTTTGCAAATGTATCACCATGCAAATATGCATTGT  
TTTCCTGACAATCGTTGTGCAGTTGATGTCCACATTAAAATACTGGATTT  
TCCCACGTTAGAAGAATGTTTAAATTTAGTATATGTGGGACAAAGTGAA  
GACACACAGATTTATACATGCACATACTTTTCTTCATTCATTCTTTGTA  
CTTAAGTTTAGGAATCTTCCCACTTACAGATGGATAAATGGGTACAATGA  
AGGGCCAATAGCCCTCCCTGTCTGTATTGAGGGTGTGGGTCTCTACCTTG  
GGTGCTGTTCTCTGCCCTCGGGAGCTCTCTGTCAATTGCAGGAGCCTCTGA  
GGAGAAAATTGACCTTTCTTGGCTGGGGCAGAGAACATACGGTATGCAGG  
GTTCAGGCTCCTGACGGAGTTGGGGCAACCCTGGAGATAAGCTCACACAA  
CCCTGCAAGACCAGGTGCTGTTACCCTAGCCAATCTCATGGATGAACCA  
ATCAATGCCAGATGAGCTCTGCCTAAAATGATTTTTTGGTGAACTCTGAA  
AAGTGGAATATTGTTTCTGTAAGAATATCCATCTGAGACTCTATCTCTTG  
GTAATAGCAAGAGTTATCAGTTTCTCTTTAACCGAGACACCAGCAAAGTG  
CCTGCTCCAGGGTAATGCCAGGGGAGCCCTCCATTTGTAGAATGAATGA  
GAGTCCAGGTTATGAACAGTGCCTGGAGTGTAGGAACACCCCTCCTTTGCC  
TCTTTGACAGGTCTGCATCATAACACTTTTTTTTTTTTTTTGAGACAGAG  
TCTCACTCTGTGCCCCAGGCTGGAGTGCAGTGGCAGCATCTCGGCCCCCT  
GCAAGTTCGGCTCCCGGGTTACACCATTCTCCTGCCTCAGCCTCCCCA  
GCAGCTGGGACTACAGGCACCTGCCGCCACGCCCGCTAATTTTTTGAT  
TTTTAGTAGAGACAGGGTTTACCATTGTTAGCCAGGATGGTCTCGATCTC  
CTGACCTTGTGATCTGCCCGCCTCGGCCTCCCAAAGTGTGGGATTACAG  
GCGTGAGCCACCGTGTCCAGCCTGTAAACACTTCTTATAGCACTGAGTTGA  
AACCTTGCTCCTCCTGGTTCCTCCAGGAACTGAAATCTTTTTGAGCCAA  
GTCTAGCACAGTGCCTGGCATGTACATTCAAGGTGGTAGAGTTTGCTGCTT  
GAATGGGTGAATGGGAATTTGACAGCATTTTATTCAAATTAGTATGTGC  
CAGGTATCGTGTCTCGCTCTGCATTATCCAAGGGAGTGAGCCTCTGTGCAA  
GTATTTGAGACACGAGGGAATAGGTTCTACTGTGGGAAAAAGAGCATT  
CATGGACTTGCTCTCCAAGCAGCCTTCTGATTTTAAATTTGGCTCCAGT  
ATCTTGATATCAGGAGTCAGTCACAAGAACTCCATCTTTAGTAAGTTATA  
TTTTCCACAGGAAATCTAAAAGCTGTTCAACATGTTAGTTTCCTGTGAAT  
TTGATAAGCCATAATCCATTCCCTAACACTGAGCCCTCCTGAAATTTGGTG  
TCTGGTCTGTCAGATAGCTAAAAGCCCTGTCTGGGTGGCCTAGGGACTCC  
TCTGTTTTGCTCCACAGGATCCACTTTGCAAATTAACCACTGGTTCTCC  
CGTTGTAGGAACGCCACCTTCTCAGAGCCTGTCTTTCTTCTCTCTCTC  
CTTCT  
CTTCT  
TCCTTTCT  
CTCCCTCCCTCCCTCTCTCTCTCTCTCTCTCTCTCTCTCTCTCTCTCTCT  
CTTCT  
CTCCCT

FIG. 3 (44 &amp; 52)

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TCTACCTTTTATCCCCCAGCTGGAGTGCAGTGGTACAATCATGCATTCAAT  
TGCATGATCACAGCAGCCTCAAACCCCTTCTCAGAGTCTTTATGCGGCAA  
CCAGCAGGGTCTGGAGGGTTGGTGGCTCTGTGAACCTCTCTGACAGAACA  
CAGAGATGTCTTTGGTCTGTTGATGTGATTACAAGCTGAACGAAGGAAGA  
TCAAAGCCAGTGACAGGAAGGGAGATATGCAAGGGACCCGAGCATCAGCT  
CTGAGTTAGTCCATTCTGCTTCTGGGACTTGGGATACAGGTGAGAAACCT  
TGAGCTTCTACTTCTCCATCTTCCAATTGTAGCATCCAGGACCTCAGAAT  
CTGCCAGCTAAGAGGAGCCCTAATGATTGTCTGGTGGGATATGGTGGGAC  
CACAGAGATGAAGACATGAATAGCTATTTGAATGTGAACAGCAGACGAAG  
AAATCAAGGCTAGGAGGGTGAAGTGAAGTCACTCATCCAATAGCACAGTGTGGT  
TGAAGCAGCACTAGTATCCAGGTTGCATGAGCCCTGATGCTTTCGCTCG  
AGGGAAATTTTGGAGCCATGGGGCAATGCCCCCTGACGTAACAGTCTCCA  
CAGTTCTGCCATGTCTCATCCTGGCCCTGTAACCTGGACCCAAATCTGCT  
ACCATCCCATCCATCTCAGGAAGTGAAACCTCTTATGTCAAATAGGTTGT  
GCAACGTATGTATCAGATCCTGTCTTCCCAAGGAGACCGCTCAGGCCACA  
GCACTTCTCTCCGATCCCCAATGAGCAGAAAATATCTCGCTATAAACATA  
GTTGGCACTAAGGGAGGGAGTGAAGAGTGATGATGATGTAGATGGTGTAT  
GTAGCCCCAAGGAAGTGAACAAGCAGAGATGGGGAGCTGGAAATGCCAG  
GATGCTCCAGCTTTTGGGGAATTATTAGCTCTTGAGTCACTAAAGCCTT  
TCTCAGCTGCAAGTTCTCTTACCCTGTGAGGTCACTTCTTCCAAGACAG  
GAGACTGACATTTATTCAAAGCAGCAAGTGCCCTGATACCATCTTGTGTC  
TAATCATGGGCTTCGCAGCCAGTTATCAAGGTTGATCTCATCTCATTGGT  
CTTCAATCATTTTGAACAAGAAGACAAGCAAAATAATCATGGGTTAGTTC  
TTATATTATTGTGTGTACATGCAGTGATGTCTGTTCTTTGTAGTGAGCTG  
TTCCTTCTCTGTTCAACCTCTTGTCTTAGAACAGAACTAAGCAATCTGCCC  
CCAACATTTTCCCCAATTTCCCATCTCATTCTTGGCACTGGCTTCTTAAT  
ATTTGTTCTTATGAGTCATTTCTTGTATCATTTCCATGAGTCCCTCTGG  
GATCTTAAAGTATGAAAAATGTTGTGTGTACCCACACCTGTCTTTGTGGA  
TATTTCTCTCTCTTCCCTCTGCTTCTGGGATTATTTGGGAATGGGCACT  
ATGATTTTTTATCATATCGCTTCCACTTCTTTATGGCATCATCTCCAATG  
GGCTTCTTCTCCCTCTTGGATCCAGGTTCTCAGATTGGGGACATGCAGAG  
TCCAAGGAACATTCCATTCTCCTCCCTGGTCTAGAACAAGGAGGGCTTAG  
ATATATGAGCAGGTGGCTGGGGCTGGCGAGCTATGTAGTCTCCAATGGCT  
TTTCCCTGATGTGCGAGTTGTTATGTGAGTTCTGGGAGACCAATAAGACC  
TTGTCTCTCTTTGGATCCATCAGAAAAAGCCCCCTGGGTGGGTAAAGATGG  
ATGGCAGGGCTCTCCTACTCTATGTCTTTTCTCACACCTAGTGGGTATAA  
GAGAGGGGACCACAAACAGAGGGGGCTCTGGTACCACCTTATCCAGGGTCT  
GGAAACATTTTCTGTAAAGGGCCAGATAATAAATGTTTCAGGTACAACCTA  
CTCAACCTTGCATCATTTAGAAAAGCAGTCAGATAATACATAAATGAAT  
GGGTGTGGCTGGACTTGTCTGCGGTCCCCTGTCTTATATCATTGTATTA  
TATCATTTTTTCTTACATACAAATTTAGAAGCAATACTTAAAAAAAAAAAA  
GCCGTCCTTTATTGAGCACCTACTAAGTGCCAGGTACCTTTTTTCCCTC  
ATTATCTTATTAACCTTTTATAATAACCTTTTAAAGTAGATAATATTGAAC  
CATTTGACCTATGCAGAACTGAGGTTGAGACAATAAATTATTTAAGACC  
GCACAAACAGTAAATGCTGGAACCTACGACTCAAATATGGGTTAACTGAAC  
CAAAACCAGATCTTTATTTCTCACTTTTAAATTGTTACATATGTTTATTGC  
CTCATCTCCTGTCCACATGGTGCCCATCGGCAGACTCCTTTCTCATTCTC  
AGTGATTGAGTGACATTCTAAACTACATTGGCCTGGCAGATTACCTCTG  
TCCCCTAAATGTTTCCACATTGTCTTTTAGGATTGAGATCCTCTCTGTT  
CCCTTGTCTTCCCTCCTTTCTTCTTCTGGCGGTGACGTGCTGTGTGAATT  
TGTTTCTTTCTCCTCTCAGGGTAGTACTGGGACTTTCCAAATCAGGGTTT  
TTAGTGATCTCTCTTCCCTTTTCTGAGTTTCTTCTTATTCCCATTCCT  
TTCTCATCTATAAGTGGCAGCTTTGTTGCTGGAGGATTTCTTTGTCTT  
TTATTCTTCTTTAAGACTTTGTGATAACTGTCAAAAGCAATCCCTTGAAG  
GTATCTGTCTTGGAAATTGTGTGCTTATGATGCTGAAAAATACTCTCTTC  
CTAAAGCTATTATAAATGCT

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GGCTAGCTGCAACTCTTGAATACAAACACATTGACATGCACACACTTT  
CTGGCTCCCAAAAGAAAAAATAATCAATTTATAATAATTCTGATCTT  
TTGCTTATTTCCACAACTCCATGAAAATTGTACATTGTCCAAGCAACAT

FIG. 3 (45 &amp; 52)

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TTCTTAATATTCTCTT...TCTCTCATATCCATTTTCCTTACTGCTGTC...  
CACCTATCTCTTCCAACTCCCTGTTAAATCCCTGCCCCAGCGAACTTT  
TATTCATTTTGTGGAATGGAGGCTGCACTGATTAAATTA  
AAAAATCCCTACTCCATGTCCAGATCCCTAGTTGTTTTTGT  
TTTTCTGAGACAGGGTCTTGTGTCTTCCATGCTGGAGTGCAGTGGCATG  
ATCATGGCTCACTGCAGCCTCAACCTCTGGGCTCAAGTAATTCTCTTGC  
CTCAGCCTCCCTAGTGTGGGAGTTCAAGGTATGTGCTACCATGCCTAGC  
TAATTTTTCTTTTATTTTGTAGAGACACGGTCTTGCCAGGTTGCCAG  
GCTGGTCTAGAACCCCTGGGCGGACGTGATCCGCTGCCTCGGCCTCCCA  
AAGTGTCTGGGATTACAGGCGTGAGCCACTGCTCCCGGCTTGGGTGCAA  
TTTGAGCTTTCTCACTTATTAGTGTAAAGACATACAGCTAATTTCTAAATC  
TTCCAAACCTCAGATTTTTTCATCCATGAAGTGAGGATTATTATAGAGCTC  
ACTAATAACATGGCTTCAAAAATATATAATGCCAAATTTGAGATCAAAAT  
AATAAATCTATATTACATGGGAGATCTTAATGTACCTCTTATATTATTGA  
TAGACTAAGATGATCAAAAAATAGAAAGAGAGCAGTAAGGAGAGCAAGC  
ATTTAATCAATAGGACCAATACATTTTAATCAATAGGATCCTCAGGAATA  
TATACAGAATACCAACCTAACAACTGCAGAAAACATGCCAAACATTTAG  
GTACAGACATTGTGTGGAATGCAATCTTGAAACGAGTGGACTGACATTC  
AGAAGATATTAATAAGAGCACTAATGATGGGGATTGCAACCATGTCTTTA  
CTGACTTCCAGAAGCTTCTTACAGTAAACATGAAATCACATAATTTCTTC  
CACTTTCTACTGTTTCTTGTCTGGGCTCTGTCTGCTTACTGTCTAAT  
ATCTTGGCCCCCTTAAAGTTGCTAATCTTCCAAACCTCATTCCTGTGACT  
GGGCGCTGGTCTTGTTCATGGGCTTGAATACTGACTGTACACTTA  
TCTGGAGCATCCAGTGCCTACCACCTGACCCAGATTCCTCATTGCGCTCC  
TCCCTCTCCACCTATTGGAATTTGCTCATACCCGTGTGAGACCCCTCC  
TTTCCCCCATCTGAATTTTTATCAAGACAACGCACTGCCATACTCCCTC  
GTACCCTGCTCTGGGCATCAGACTGAATGTTTGTTCATTGAGGATCTG  
CAGCTGCATCAGTTTCCCCAGCACCGTCCAACCCCTTGAGCATGGCTAGT  
CCTAAAGCAGAGAATTAGCCTTTCTATCCCTGCTGCTATACATGCTGGGA  
CAATAATAAGAAATGACAGCATTTTATGATAATGCAGGCTGCAGGAGGC  
AGGAGGCAGGAATCAAATTCGTGCTTATCAAATAGTGCTCCAATTCCTTG  
AATATTGGACTATAGAATATGTCATGGATCTATGCTCAGGTGGGTTCCCT  
ATTACTCACTCCACTGAGGCCAGGTTGTGGGATTAGCTGTCCAAGAGGGA  
GTTTCAGTCTCACAGCATAGGGTCATTCTGAGAATTACTGGCCCACTT  
GTGTGGAGACCTCCAGAGAACAGAATCTGGGTGGTGCCATGTACTTCCA  
GGAGGAGAGAAGTGGCAGGATGCCAGCCCCACAATCAGAGGGGAAGGGG  
CAGAGCCACATGTATGAAGATCCTCTCCCCAGTACGTGCCAATCACAGGG  
CTTCTAGCTTTTGGGCCAAGGAAACAATGTGGGAAGCAAAAAGGACAA  
TTTTCTCTCCCTTTGCATGAAGACTGAGCAGTTTACCAGATTCCAGG  
GAAACACCTTCCACTCTGGGTTGAATGTGAGTGAGAGACATTCACTGG  
AACACTAGAAAACTATTTCTGAGCCACTCACCTTTAGCCCTAGAAAGT  
GTTGGATTTGTCTTCATCTTTGCCACAGTAGAGACTGCTGATAGCATCA  
GAACCTTGGGCTCTGGAATTAGACAGATATGGGTACAAATCTGAGCTCTCT  
CACTTATTAGTGTGGGATGTAGAGCAACTTTTAAATCCTTCCAAACCTC  
AGACTTCTCATGCATGATGTGAGGATTGTAATAGGGCCACCTAATAGGG  
GTTTTTGAGAATTAAGAAAGTTATTCAATGAACAGCATTAGCAAGATGC  
CTGACCATTGAGAAAAATAACAAATTGTTTATTATTATTGTTATTATTA  
CATCTTTCTGCACCTTCTGACTGGGGGCATCGTATCATCAGAAATACTT  
AGGATGGGATGGATTCTGCTATGGGCTGAGTCAAGGGTGCAATAATGGAG  
GAGTGAAGAAGGAAGAAATGGAGGCAGAAATCCCCAGGAGCCAGCATGG  
TACAAGGCTGAGCTAGTGTGCTGAGAGCCTCCTTGGAACAGCCACAGAGCT  
TGCTATCTGGCCCTGGGAGGAACCTCTTCTAGCTGGCAGGACCAGCCCAA  
CAGTGGCCAGGGGATTTCCAGGGCGTGGGCTCCTAGGAGTTCAATTGGA  
CCAAGCCTGCCTGGAGAGGGGTTATAACAGGGATCCTTCCCTACTGGCAG  
GTGATTTACCCCTCGGTGAGAAGCTCAGGCATTTGTTTGATGGAAGGTGG  
AAGGCCCTGTGCTGGGCCAGTACTATCAGGGATGGGCGGGTGGCTGGAA  
AATAGCAAAATAGACAATATGATAACACAGTTAACACCACACTATGTGA  
AGCTACAATATGGGTATCTGTAATAGACAATCCAATGTAGAGAATAATT  
CTAAGGTGTCTCTCCCCGCAATGCCATAAGCACAGGCCCTCTGCCTG  
GGTTTTCTCACTGTGGAATGTCTCTGGTCTCTCATGCCAGAGAGTGG

FIG. 3 (46 of 52)

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GAAGTACTCCTACTTT. .CACCGGCTTTCCTGTCATCTCCCTGCAGCC...  
CCTCAGCCCCCTCTGCACAGGGAGGTTTCCTCCCTGCTGCTGCAGTGCTT  
TGTACTTGTAGTGGTACCTGCACACAGGTATTGGTGTCTTGTCTCACC  
ACCCTACATCACTGTAAGCTCCCCAGGAGCAGGCTTCTGTTTGACTCAC  
CTGTGATCCTCCACCTCCACCTGTAGTGCCTCAAGCATTGAGGACAAT  
CACTGGCTGCCCCCTTAACCCAGAAATGCTGCCGAGACAGGAGGCCATGGC  
CCAAGTTCCTGGAATGGGGTATTACTATGTCAGCACAAAGGCCTTTGCAC  
AAATGAAGGCTTTAAAAATGCAGTCCTAGTCAGGTGGAGGAGGGCTTATA  
GGATTCCCAGGAATCTGGATCATTCTCTTGAGAGCTTTCCTTGTCTCTG  
TTAAACTCACATCCTACGGCCCAAATAACAACAAAAATGGATGTAAAT  
TCTTGAAATAACTTGTGGATGGGGGAACAAGGCCACCCCCCAGATCTGC  
CAGAAGCTTCAGGTGAGGGTCCCAAATGCCAAAAAGTCTGGTATCAGAGA  
GGATGGCCAGTGACCTGGGGACACATGCCCTTTGCTGTGTCACTCAAGGA  
GCAGCAGCCTCGGCCCGCACAGTGACCAGGACCCTGGCTTCCCACGCTG  
GGCAGGAGCTGGTGTCTGATGAAGGGAATGCCTGGCAGCACGTGCTGTCT  
GTCTCCTCGTGCAGCTTACCTGGCTTTGCTGCGAAGAGGCCACTCGCAT  
TTCTCAATTTTTTATATTTTTTTAATTTTTTAAATTTTTTATTTTATTTT  
TATTTTATTTATTTATTTATTTTAAATTTTTTTTTAAATTTTTTAAATTA  
TGCTTTAAGTTTTAGGGTACATGTGCACATTGTGCAGGTTAGTTACATAC  
GCATACATGCCCATGCTGGTGCCTGCACCCACTAATCGTCATCTAGC  
ATTAGGTATATCTCCAGTGCTATCCCTCCCCCTCCCCCACCACCAA  
CAGTCCCAGAAATGTGATGTTCCCTTCTCTGTGTCCATGTGATCTCATTG  
AATTTCTTTTAAAGTGAATCTCTCAGTGGGTCTAATCTGTTTCAAGAAAT  
ATCAAAAGAGTATCCTTGGAATGACTGGAATTCAGAGTCATCTGGTAA  
TCCTCATAAAACAACCTCCTGGATGTCTCTCAGCACATCTCCACCTTGAA  
CGCAGGAGGCTGGTTCAAATGGAGGAGCATCGCTCTACTGCACCTTTTTT  
TTTTTTGGCCCTAAAGTGCAAAAGGGGATACGTTTCATGTAAATAAATCA  
ACTGCAAAATCGCTAGTTATGCTGAGCCCTGTCCCGTGTGTGGACACAAA  
GGAACCAAAGGCTTTTCTCCCCGCCCCAACACACATAACACACACACAA  
AATCATAAAAACATACATACCCCAACACATAACAACACACACACACAC  
ACAAAATATATACACACACACACACCAAAACATGCCACAAACCTGTGTC  
CAGAGATAGATCCTACTGGTGGGTTTGTGGTCTCGCTGACTTCAAGAATG  
AAGCCGTGGACCTTCGCAGTGAGTGTTACAGCTCTTAAAGATGGCATGGA  
TCCAAAGAGTGAGCAGTAGCAACGTTTACTGTGAAGAGCAAAAGGACAAA  
GCTTCCACAACCCAGAAGGGGACCCAGCAGGGTTGCTGGTTGGGGTGGC  
CAGCTTTACTTCTTTTGGCCCCCTCCCATGTTCTGTTTCCATCCTATCA  
GAGTGCCCTTTTTTCAATCCTCCTGTGATTGGCTACTTTTGAATCCTG  
CTGATTGGTGCATTTTACAGAGTGCTGATTGGTGGGTTTACAATCCCCT  
TGTAAGACAGAAAAGTTCCTGATTGGTGTGTTTTACAATCCTCTTGTAAAG  
ACAGAAAAGTTCCTCAAGTCCCCACTGGACCCAGGAAGTCCACGTGGCCT  
CACCTTTCAACTCCATAATGGCATGAAAAATACATATGTTGTACAAAACAT  
ACATACACAAAGTATACATGCATCTCCCCAAATATACACATAACACAGAA  
ACATACACACAGGAACCTCAGCTACCTGTCAAAGTCTGCATGGTGATTGC  
CTCTGCAGTGAGTAGTTAGAAAAGTGAATTTGTTTTTCAATAAATTGGAG  
TCCTTAAAAATCGTTGTAAGATAGAAAATTTTTTAAAGTATATAAATAA  
AATATGTATGTCCTTTGGTCTAGCATTTACACATGTAGGAATTTATCCTA  
GTGGAGTAATCAATGATATATGCAAAGATTTGGACAAGCATATTAAGCAC  
AGAATTATGTATGCATATGTGTGTATATATATATATATCTCATACATA  
TAATAATGTAAAAGTGAAAATAACTCAGATGTTCAAATTTGAGGATTAGT  
TAGACTATGATCTGTCCATATGTGACATAACAAGTTAGCTGCCCCCTTATTC  
TCTCGAGCTTCAACCTCCTATAAACAGTGTCCCTTGATATATCAGTATTGG  
TACAGATAATCGAACTTATTGAGGTTTTACATGGGGCAATAAAGGCAAGA  
GTTTATGAATACTCCATACTACACTAGGTAGCACCCCTATTAAAGACAA  
ACTCTTCTCTCTCATTTCCCTTCTTTCCGGAACCACTTGGTTGAATCTC  
TACAAGTCTCTATTGCAACTGCCTCAACATGGCACCCCTCCCTGCATCTCC  
ATCTTCCCTGTCTGAGAGCAATGGCCTGCTGCCCCACACTCACATCCT  
CATTTCATTCCAGAAGTGAGCACCACAGAAGTGCTACAGTTACCCCAACC  
ACCTCTTCAAGATAAGTTAGTGTGTTTGGTGTGTTTTTAAATTTTTTA  
CTTCTCTTTTCTTCACAATCTCATCCCATCCCAAGAGGTTTATCAAGA  
AGTTCTCTAAAGATATGTGTCTCCTTATGGAATTTAACAGAAATCAGGGA

FIG. 3 (47 of 52)

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TTGGATTCAGCCATCAGGGAATAACATTTTTCCAGGTCTTTAGAC  
ATAATGGAATACCTTGCAAGTAATTAGATACACTATTGTAGAAAAGTATTG  
ATGAAATGGAACGATGTTTGAGATATCATATTGAGTAGAAAAGGCAAGAT  
ACATTAAGTAGGAAATGTATCTTACAAAATAATTTGTCAGACACACTCCT  
ATATTTGTATGTTATATAAATGCGTATGTGAAGAAAGGCTAGAGGATGAG  
ACCACAGTCTTCGGTGAAGTTTAAGAGATGATGCTGCAGCATGCTCAGAA  
AGGCTTGGTATAGTTTTTTCCAGTAATTAAGGACTGATCTTAGGTAAATT  
GTCCATCCTCTCTAACTGCACCACCTTTTGTCTGTAAAACAGGAAGGAT  
GGTATTTACCCCCAGGGTCATCAAAGGATTTGGTTGGAGAAAAATAAATA  
AATGGGCTGAGCCAGACCTGGCACAGTGAGAGCACAGTGGTTGACTATT  
GTGCTGGCCTGTTGTTCTGTGTTATTGACATGCTGCTGGTGGTGGTCCA  
GAAGCTATTACCTTAATTGGTTATGTGGATTTCCCTCATACTGAGCAGC  
TGTGTGTGGTGTGTGTAACATAGCCATACACAGTAAGTACAAGGGCAA  
ATGTGATGGAATAATGCAAGGAAGTGCAGATAAATAGCTAATGGGCTGTA  
GAAGGAAGCTAGTCTTGGAGGGCTTGATCAAGGAAGGTCTTTTGCATG  
TCACCTTTGAAGAAGAGGGGACATAGAAGAGGTATAGTGCATCCCGGAGT  
GTACCTGGAAGGACATGAAAAGAGGACATTTTTCTCTGGGACATGGGG  
ACTCCACTTGCACTGAACCTCTGGAATTGGGCAAGAACCATCATGAGAAC  
AAGGGCTTCTTGAACCTCCAGGCTCATTGGCTGATCTAAACCCTGTGT  
CCCCTCTTTCTTCACTCTCCTCTGTTTTCTATACCTGTATTATTGGACT  
GGACTGGAAGCCACCTGATCTATCACAAGTACCTTGAAATGTGTTGAATA  
GGTGTGGCACAGTCTTAGCAGAGTGGCACTACCCCCACAGGAATTTGTT  
TATACCTTTGGCATGGAATAAGCAGGAAATGAGTGATCACTGATAACTG  
AGGATGCTATTATTATTGGCCAAAGGAATACCTGTGTGTGTTTGCATA  
ACCACTCACAAACTGTTGATTACAAATGAGTACCAGACCTAGCTCCTTCA  
AGTAAAGGATCTTGAGAACTGAAGGCAACAGAGCTCCAGGAGTCCAAGA  
CAGAGCCACAGACCACGAGGATCCCTGGCCCAGGTAGGTGGTCTCTCTGC  
ACTGGCTTTCAAGGCCAACAGGATGGATGGGGAAGTAGAGTAGCATCTGG  
CCATCTAGACCCTTGCTTTTTATCCCCACTGGAAGCACATCTGAATTTCT  
AAATATGATCTCTGAGACCTGCCCAGAACACCTTGCTCTCAGCCCCAGTA  
GCAGCCTGCTCTCTCCAGGAGGGCTTCCACTAACAAAGTAGGGCATTGCT  
GGAGGGCCAGGCAGACCTAGCTTAGGAAATCCACCAACCCTGGAAATGC  
TAGTCCCTTCTCTGAAGGCTCAGAAGACTGACTTTAGAGTCTAGAAAATA  
TTGGTCTTTGGGAACAGATTTTGAGTGCAAAGAGATGGACTTCAGATGGC  
CAGATGCACTGCTTCTTTAGGGAATCTGTGAAAGCTCCCTGCATTTATC  
TTAATACAGGCAGCAGATTTTATGAGTACCCCGAGGGATGGCCCCAGGT  
CCTCCAGCCTGTGAGCATCCTTCTGTCTTCAGCAGCACCACAGTATCTT  
TATATGCTTTGGATACCTACGTTTCTGCCAGACATCTCTTGCTCTGATG  
TTCTGGCTGCCAAATCTCTGTCAAGCGCCTCCAATTTTTGTGTCTTT  
GATTTACCCCAACATGACAAAGGCAGTTGTGCTTCATGTATTACAGGATA  
CTGCCAAACCACAAACAGGTTAAATCAAATAGCAGATATCCCTGTTCTT  
AAAGACCCATCAGCTCTACCCACCTGCTCCTGCTCACCGTCTTATTGTT  
GAGTCTGAAGCCCTTCTTGTCATTTTTATTTTTTGCATGAACAATTTA  
GTTCCCTTTGTCTCACTCCTAAACCTTTCTCAAAGGATTGGATTTGTACA  
CAAACCTGCTATCTCTGCAATCTTAGAAGTGATATGATTCTGAACAAATC  
ACTTAACTTTTGATTTTTATTGGTAAGATGGGAATACCAATTTTTGCTC  
CACTTCTGTCTATGTTGGCCTGGGCTGATGTTGAAAGCTCTCGGTCAAC  
TGAGATAGGGTGTGCAAGATTTATATATATAAATATATCTCCTCCAACCC  
CTCCCAATGAAGCAAGTCACGTGAGTCAATCCTACCTAAGATATTAGGG  
ATTGAGCCTCCTGGGACATTTGGTGGCTTAGGTTTTCATGAAAAGAGGTT  
GCAGAGCAACTGCTTTTTGTTAGGCAAAGATTAGGCTACTGCAGAGACTC  
AGCAAACCTTATAGAAAGGTGTCAGATGGTAAGTATTTTAGGCTTTGCTT  
GCCAGATGATCTCTCACTAGTTAACCATGCTATTGTAGCCTCGAAGCAG  
CCAGAGACGATCTGTAAACAAGAGCATGTAGTGTGGCATAAATATAGTA  
CCGCG

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GCAATAAGTCTATTTACTGTAAAGTTAATCAAATTTACATTTCAGAACAC  
TTAATCTGCAAGAGTCTTTCCAAGACCCTATACCTAATTTGTGTTTAC  
AATTTTATATTGTTTTCTTAAAGAAGACCACCAATATAAACTATATCCA  
GCTTCATGATAAGTACATAAGAACTATGCAATAAGGGGGAAAAA

FIG. 3 (48 of 52)

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CAAAGAAAAATACCTAC TACTAATGGTTCACCTCTGAATAGCACAT...  
TCATAATGATACAAGCACTCATTACTAGTCTAGGAAAATGAAGATATAAT  
TGCATTAGGAAGATCAAGAGGTAGGAAATGTGGATGTGTGTGGTATAGAC  
TAGGGCAGGACAAAGAACCTAAATCCTCATTCTTCTAAAGATAATTGTAA  
TACGTAAAACCTCAAAATTCAAGAAGTAACAGTAAAAGCGGTCATTAAGAA  
ACAAGCACTAAACACCAGATAGGAAGCGAGAGATGGGGGAAGAGGGCAAG  
AATCTGATTATTTTTTGAACAAATTTTGTAAAACCATTTGACTGTTTAC  
ATGTAGAACTTGGATCTTTTTTAAAAAACACAAAATAATAACTATTAT  
TTTTTAACCTGGATTTTTTGAAGAAAGATAAAAAGTCTCATTTTAGTAATT  
AAAACCTCATTCCAGGTTAGTCCACTCAAACTTATATTGAAAATTAATA  
CTTTGGGAGGCTGAGGCAGGCAGATCACCTGAGGTGGGAGTTCGAGACC  
AGCCTGACCAACACGGAGAAACCCCGTCTCTACTAAAAATACAAAATTAG  
CTGGGCGTTGTGCATGCCTGTAATCCAGCTACTCGGGAGGCTGAGGCAG  
GAGAATTGCTTGAACCCGGGAGGCAGAGGTTGCAGTGAGCCGAGATCACA  
CCATTGCACTCCAGCCTGGGCAACAAGAGTGAAACTCCATCTCAAAAAAA  
AAAAAATAAAATTAAAACCTCTGGAAGTTGAGTTTGCAGATATTAT  
TATGCTCATTTTTAACTTGTATGTTTGGAAAATGTCATGATGAGAATTGA  
GGTTGGGGGATGAGAAAAAAGAAAAACATCAACCCACAGCCCATTCAA  
TTTTCAGCCCCGACCCACAGCTCCGGGGAAGGGCAGCAGGTCCATCCTTCA  
CTCTTTCTTACCTCTTTCCCTCCTTCTGGCTCTTCCACCTCTAAGTTG  
GAGCCCAAGAAGAGGCACCTGGGAAATGGAAGTCTTTTGTACGTGGTAC  
TTGCCGGGAAGCTGCCATGAAGACCTGGCCCCACGGTGGGGAGGGAATG  
CCCAGCTGAGGCCTCGTGCCCATGTCTAGGATAGACTCGTCCAGACATGTC  
AGGTGGTCTGACAGGGCAAGCAGCAGGAAGTCATGTATGAGTATGAACTG  
ATCTGTATGCAAGGGCGGGGAGAACACGCGGAGGAATGGGGCGTGAGAAA  
ACAGCACAGTACGTTTCTTTAGCAGCTGTCTCTGCTCAGCCATGGGAGTC  
ACCAGAGAAAGAGGCTTGGAGGCGTTATTTTCACTGTGAGATGTGAGTGT  
AAAAAAGTGCCCAAGACACAGTGAGTACCAGGGAGATGCCCTCTTTCCCT  
ACCCGAATGCAGAAATGGCCACAGGCCTTAAACACACACATGGTTCCCTCA  
GAGGAGAGAGGCCTCCACAGTGGACACCCGCATTCTCCCTGGTCAGCAG  
CAGCAGGGCGAGTGCTGGGCCATCATGAAGCTTACAGGCAATGAGCTCT  
CAGCAATAACAGGAACAGTGCTGGGGACTGTAGCTGCAAGACCGATT  
TCATGTAAGATGGCCTCTGAGGACTCCGAGATACACCAGGCTGAGACTAG  
CTGGCAGCTCCAAGTTCTTGGTCAGAAGAGAACAGGAAGTAGGGAAATTG  
GAATTACTGTTTACTACAATTCCTTTACATCCGCACAACCATGAGGTCCAG  
AGAGTCTGCTTATTATTTTTTTTAAAGACAGGGTCTCACTCTGTGCGCCA  
GCCTAGAGTGCACTGGTGTGATCATGGTTCAGTACAGTCTTACCTCCCA  
GGCTCAAGTGACCTCCTGCCTCAGCCTCTCAAGTGGCTGGGACAGCAGT  
TGCATGCTACCAGGCCTGGCTTTTTTTTTTTTTTTTTTTTTTTTTTTTT  
TCGGTAGAGACTGGGTCTCTGTATTGCCAGGCTAGTCTCGAACTCCT  
GGGCTCAAGTGATCCTCTGGCCTCAGCCTCCCAAAGTGTTGGAATTACAG  
GCATGAGACACTGCACCCAGCCAGTATAGTCTTTTAAACAGCTTTATTGAG  
GTACGGCTAACATTGAAAAAACTACACAAATGTAAAGTATGCAATTGAT  
AATTTTGACAAATGTACACACCAGTGAAACTATCACTACAGTCAAAATAA  
TGACATATCCATCACTCCCAATTTCTCAGCCCCCTTGGTAACCCCTCT  
CTCCCAACTCCCTGCCCTTAACATCAGACAACTACTGATGCATTCTGTC  
TCCATAGGCTCATTACATTTCTAGAATTTTACATAAATAAAATGACAG  
AGTATATACTCCTTCATGTATGGCTTCTTTCAGCCCAATTATGTCAAGAT  
TCATGCTTATGGCTGTGCGTATCCTTAGCCCATCTCTTGTCTTGCTGAG  
TAGGATACCATTGCATAGACAGACCAGCTTGCTCATCCATCACTCTT  
GACAACGTTGAATTGTCTCTGTTTTTTGCAATGACAAATAAGGTTGCTAT  
GTACATTCTGTATAGACATTTGTAAAAGCACAGCATTTCAATTTCTCTTG  
GGTAAAGACCTAAAAGTGGAAGGCTGAGTCATATGGTAAATATATATGT  
CTAATTTTTTAAAGAACTGTCAAACGTACCCAAAGGGATTGTACAATT  
TTACATCCCCACCAGCAGTGTATGAAAATTTCCGTACTTCCACATCCTCA  
CCAATATATGGTGTGGTCAATCTTTTAAATTTGGACATGNTAATGAGTG  
CAAAATGAGGCCCAGAGTGTCTGAAGTTACATTTGTATCCTTTTTTGGCAT  
CCAAAACAGGTGTCAAGCATAGAAAAAACACTTGTTCTTGAATGGTCAG  
TCATTTACAAGTGGAATTCATTACAAACCGGTAGTTCTACTGGGTAAAC  
TATGCCTTACTGTCAACAGGCACATACACATACAGACAGACAGGAAGGCA

FIG. 3 (49 of 52)

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CAGAGACAAGGCAGAGC...TGATAAGAAGGTGACCTGGGCTCTAGCTCT...  
GCCTATCACCTAGTAAAATATTAGTTAAGTAGCCATGAGTAACTCACTTA  
ACTTACCACAGGCTCCATTTTCTTATCTGTAAAATAGGAACATTGAAACA  
GCTAATCCCCAAGGTTTGTGGATAATCAGAATTACAAAGATCAATGACAT  
TTCTATGAGAGAAACATATTTCCAAGTATTTGATGGAGTACATCAGACAC  
AAAGGAAAGGAAACTGAATATTTTGGAGTTTCTTTTACCAAGAAA  
TTCACATTTTGTAAATTTTCAGAACTACCTCCTGAGGAAAGTGTAGCTG  
CACCCATTTAGAAATGATAGAAAACATCAATCTGTCTGATTCCAAAGCCAA  
GTTCTTGCTACAAACGAGAAATGAAACAACTGGATCCCTACAGATGCAGAG  
ACCTGGGCCCCACAAATGTGAATTCTGTTCCCTACCGAATAGAGTTACA  
GTTCCATAATACAGTACTCCCTCACTTTTCCACAGTCTCACATTCACAG  
TTTCAGTTACCCACAGTCAACTGCAATCCAAAAATATTAATGAAAAATTC  
CAAAAAATAACAATTGAGAAGTTTAAATTTGTGCTCCATTCTGAGTAGCG  
TGATAAAATCTGTGCCACCATCCCACCTGTCCAGCTTATCGTTAGTCAT  
TGACATCGTCTGCTCCTGACATCCAACCATTGACATCATCATGACTCTAT  
GATCCAGGATCACCGAAGCAGATGACCCTCCTTCTGACATATCATCAGGC  
CAATATCAGCCTAAACACTGCATCACTATGCCACATCAGTCACTCACT  
TCATCTCATCAAGGAGGCAATGGATCACCTCACATCATCAAGAAGAAG  
AGTGGGTATAGAACAATAAGATAATTTTGGGGCAGGCATGGTGGCTCACG  
CTTGTAAATCCCAATCTTGGGAGGCCAAGGCAGGAGGATCCCTTGGGCC  
CAGGCATTCAAAACCAGCCTGGGAAACATAGTGAGACCTCCTCTCTCTGC  
AAAAAAAATAAACAAAATTATCCAGATACAGTGGTGCATGCCTGTGGTC  
CCAGCTACTCAGGAGGCTAAAGTGGGAGGATCACTTGGTCCCAGGAGGTC  
GAGGCAGCAGTAAGCTGTGATCGTGCCACTGCACTCCAGCCTGGGCAATA  
AAGTGAGACCCTGTCTCAAAAAAAAAGGTAATTTTGAGAAAGAGACCAC  
ATTCATACAACCTTTTATTATAGTATATTGTTAGAATTGTTCTATTTCAAT  
ACTTATTGTTGTTAATTTCTTTCTTGGCTAATTTTTTTTTTTTTTTTGG  
AGTCGGAGTTTCACTCTGTTGCCAGGCTGTAGTGCAATGAGACGATCT  
CAGCTCACCGCAAATCCCGCCTCCCGGGTTCAAGTGATTCTCCTGCCTCA  
GCCTCCCAGTAGCTGGGATTACAGGCGCCTGCCACCATGCCAGCTAAT  
TTTGTATTTTGTAGTAGAGGCGGGGTTTCTCCATGTTGGTCAGGCTGGTCT  
CGAACTCCTGACCTCAGGTGAGGCCTCAGCCTCCTAAAGTGCTGGGATTA  
CAGGCTTGAGCCACTGCGCCTGGCCTCTTTCCTAATTTATAAATTAAAC  
ATTGTCACAGGCATGTATTAAATTTATAGGAAATCATAGACATATAGAGT  
TGGGTACTATCCACAGTTTTCAGGCATTCACTGAGGGGCTTGGAACACGCC  
CTCCTCAGATGAGGGGGGACTACTGTCTCTCTCAATCATTCTTGATTCT  
AATCCTCAACACAAATGGTTTGGCCAGGTCTTGCCTCTGGAGACAAAAT  
GCTAAGGATTTAGAGGGGAAAAATGTAGTTCACTGGGAAAGTCACCTCT  
GCTCCACTGGACAGCAACTTAAACCCAGGCCATGACAAGTAGAAAGGCC  
ACCCCCACTGCTCTTACACCTGGAGTATTCAGGAGTCAATCATATTTCA  
GGACCACCAGGCAAACTGGGAAAAACTGAGCTGCCTTGAGGAAAGCAA  
TCAGCTCCACAAGGGGCTTAAGAAACAAGCTCTGGGAGGAGTGGTTGGAG  
AAGAGTTGGGGACACATCAGAAATGCCATCAAATTTCTAAGGGCTACCTC  
GTGGTGTGACACCTGTGCATCTTCAAGGACATAAACAGATGGGATAAGCA  
GATGAGATTCAAGAGGACATCAAATATTGGCTCCCCAGAAGGGGAGAAC  
ATTCTAGTAACAGAGCTGCCAGCTGCAGAGTGGACTGTTTCACAAAGCA  
ACAGGTGCCCTGCTCTTGAATCACCATCTTACAGGAATGCAGTAGAAG  
GGACTTAACTCCTGCCCTGAAGAAAAGGTTAGGCTAGGGAAACAGCTCCA  
AAATTTTTTAAAGGAAGCAACATAGGCATCTACTGGGAGTTTTCTAAAG  
CCTTTGTTTAAATGAACTAAAGAGCTGGGACAGGAAATGCCAAATTAAAT  
TAATAGAGCCTTGCTTTAAGACAATGCAAGTGGATGGTAATGAAGGAATG  
AGTCTTAGGCCCTTGATCAACCGTATTAAGCAATGCTGAGCATGGAGCCA  
ATTCTGTTCACTAGATTTGCTCAGAAAGGGCCAGACGAGAAGGATTTTTTC  
TAAAGGCACCTACTACCAAAAAGCTGCCAAGGCGTCCAATGGAGCCGAGA  
GAGAATATGCTAACAAATAAAAAGTTGAACACCTCAATAAAAAAGGGTAA  
AAGTAATTAATAGAAAATTACTGAAAGCTTTTTTGAACCAAAAGTAGTC  
AGCATTGGTAAAAGTCTACAAAAGTGGACACTTTCATATAATGTTGGCAG  
GAGGTAATAAAGACATAACCTTTTTGGAGGACAAATTTGGCAACAGAGTAC  
CAAAAACCTTACAATTGAAGAGAACTTTGGCCTGAGTGCAGTGGCTCACA  
CCTGTAATGCCAACACTTTGGAAGGCCAAGGTGGGAGGATTGCTTGAGCC

FIG. 3 (50 of 52)

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CAAAAGTTTGAGACCAGCCTGGGGTAACACAGTAAGACCTCGTCTCTATG  
AAAAATAAGAAAAGTTAGCTGGGCATGGTGGCATGTGCCTGTGGTCCCAA  
CTACTTGAGAGACTGAGGCAGGAGATCGCTTGAGCCTCGGAGGTCAAGG  
CTGCTGTGAGCCATGTTTCATGCGACTGTTCTCCAGTCTGGGTGACAGAAT  
GAGACCCTGTCTCACCAGAAAAACAAGGCAAGAGAGAGAGAGAGAGAGAA  
GGAGAGAAAAGAAAAGAAAAGAAAAGAAAAGATGGAAGGAAGGAAA  
GAGAAGAAAAGAAAAGAAAAGAAAAGAAAAGAAAAGAAAAGAAAAGAAA  
AAGAAAAGAAAAGAAAAGAAAAGAAAAGAAAAGAAAAGGAGAGAAAAGGA  
AGGAAGGAAAAGAAAAGCAAGCAAGCAGGAAAAGGAAGGAAGGAAGGAA  
GGAAGGAAGGAAGAAAAGAAAAGAAAAGAAAAGAAAAGAAAAGAAAAGAAA  
GAAAGAAAAGAAAAGAGAAAAGAAAAGAAAAGAAAAGGAGAGGAAAAGGAAA  
AGAAAAGGACAAAAGAAAAGACCTTTGAACCCTGAATTTCACTTTTAGAGA  
TTCATCTTAAGGAAATTCATTCCAATAGAAATTTATCCCAGGATTATCT  
AAATATTTGCTTTTATTTTCTTCTAGTAATTTTATGGTTTAACTTTCTCA  
TGTTTAAGCCTTTAATTTATTTGGAATTTATTTTGGTATGAGAAAAGTGTG  
ACCTTTTGTGTTTACTTTAAAAAATGTATTACGATTATTTTATTTTAG  
AGACAGGGTCTTGCTCTGTCACCCAGGCTAGAGTGCAGTGGTGTGATCAT  
AGCTCACTGCAGCCTTGAACCTCCTGGCCTCAAGCAATTTCTCCCTCTTCAA  
CTTAGGAGTAGCTGGGACCACAGGCATGTACCACCATGCCCACTAATTT  
TTTTTATTTTGTAGAGACAGAGTCTTGCTTGTGCCCAGTCTTGCAAT  
GTTGTCTCAAACCTCTGGGCTCAAGTGATCCTGTGCCCCAGCCTCCCAA  
AGCACTGGGATTACACGTGTGAGCCACTGCGCCCAGCTGCCTTTTATTT  
TTTAATTTTTCAGATGCTTTGTTGGTTCCAAAATAGCACTTATTAACCCA  
CGCTTTCCCTCTGGTTTAAATACTGCAAGTTTGGCTTTGAAATACAA  
CCCCTGCTTATTCAGGCTACATTCAAGGAAATCTGAGACCAAGAGTCT  
GAAGGCCAGTTTCTTCTCAAAACCCAGGAGGTGGTAAATGTGTCACTT  
CCACACTTTCTATCTATTTCTAAGAACTCCTTCTTCCAACTCTGACAT  
GCCCCCTGGCTCAGGTCTATAGAAATCCCAGGGTCCACAGACAAAGCAGA  
ACTCACTTATGGGGAATCTGGGAAATACTTATCTGTAAACCTGCCCCA  
TATGGTGACTCAGATTGTCTAAAGCCCAAAGCATATTTCCACCCCAA  
CCATTTCCCTCTCCAGACTTCTCTATTTCTGTGGTCCAGAGTCAAGATCT  
TGATATTACCCTAGAGTCCCCCTTCTGCTCTCCTGCATACCAGATGCC  
CTCCCTCCCCAGATCCATTCTCCACCCTCCCTCCCATCAGTTTGGTGGG  
CCCATCACCGCTTCCCCTGGCCAGGCTCTCCTTTTGTGCGCTTGGAGCA  
GCAGACTGATCTCCAGCCTTCACTCACTTCATGTGGTAATCTGTTGTGT  
TCATCACTGTGAGAACTCTCTGCATCCCCTCACTACTCTGCTGAAAACAC  
TCTAGTGGTTCTCTATTGCTCATTAAATGAAAGTCTAGATATTAAACGTAG  
AAGGCCAGCACAATTTGCCCTATGCCACCTACCTCTCTAATCTTTTCT  
CCTTACTCTGACAGACTCTCCGTCTGTCAATTTATGTATTCTTTTATTGCT  
CTCTTCTACTTTTAGTATGAACTGGATTTATGGATTTTTTTAACATTGCT  
TTCAAGTATGGAATAAAGAATTTTATTTATTTATTTATTTATTTGA  
GACTGGGTCTCACTCTGTTGGCCAGGCCAGAATGCAATGGTGCACTATA  
TCTCACTGTAACCTCGAATTCCTAGGCTCAAGCCATCCTCCTGCCTCAGC  
CTCCTAAGTAGCTATGACTACGGGTGTGCATCACCACATCTGGCTAATGG  
AATAAAATATTACAATGCCTAATCTTAATTTTCAAAATTTTAAATTACAT  
TGTACCTAATGCCCATGCATTTACTTTTTTCACTGGGTCAATAGCCCTCA  
CTTTGGCAAAGGTCCCAGGCCCAAGGTAAGGCCTTACTTTTTTCCAACTC  
ATCTTTTGAAGACATAAGTGCCTGTAAGTTGTACCACATTAGGTTCTAG  
GAATTTTTTCAACAAGACTTTATCAGACTATTTTCTCTAAGTTGAGAAA  
GAGCTGGGGGCAGAATATGGCACTGAATGACTGAAGAGAAGGCACTGAAA  
TCAGGCCAGAGGTTGCTGGAAAGAGCAATGAGGAACACCAGCAGCAATGA  
GGAGCCGGTGATGATTTTGGCTTCAAGGGAGGTGTGTACCACACCGATT  
TTATCTCTACGTGGATGAACCACAGCTGTCCGGCTCCCTTGTCTCCAGGAC  
ATCACACTCTCCACATTCCCTCCCATCTTCCGGCTTCTGCTTCCCGGGGC  
CCTCATCTGCCCCATCCTGGGTGAACACTGGTCCGTCAACTGCTGGGCGT  
ACCTTCCCGCTCTGCACACCTCCCTGGCCACCCCACTCTCACGGC  
TCGCACTGCAGAGGAGCCGCATCTCTAGCTCCAGCCCATCTGCCTCTTCT  
GAGCTCTAATCTATGTAGGCGACTCCTGCCGGTGTGCTTCCAGGCC  
ATCATACTTCAAAGCATTTTCCCTCAGAACACCATGTCTGGCTGCTCC  
CTCCAGAAGATACATCTCTCAAGCACATCCCCGGGCTCTCACCTGGATG

FIG. 3 (51 of 52)

ACTGCATTACCTTCTC ACATTGGCCCTCCTTTGGATGTATATAGA.  
GTTTTAAATAACAAATCTGATGTGCTTGCTCTCCTGCTTGAAACACCTCA  
AAACTGCCTTCAGGATAAACCACTGCCCTTGACATGTTACAGGTTGCC  
ATGGCCTGGCCCTGCCCATCTCTTCAGCCTCATCTCATGCCCTTGCCCC  
TCGCTCTCTGGGCTTCTGCCTCCCTAGCCCTCCTTTAGGTTCTCTAACAC  
ACCATAGTCCTTCTAGTGTGGGGCTCTGCAAGTGCTGTTCCCATTGCC  
TGAGACATGAATCCCTCTCCCTATCTCTACCTGCACCTTCATCTGATTAA  
TOCCTACCTTCTCTACTCATGATGTTGCTTTCTCAGGGACTCTCTCTGAC  
TTTTTAAACTAATCAGGGTCTCCCCAGTATATATCTTCATAGCACTCTGT  
ATTACTCCTTCTTAATGACCACCTGCTGTAGACTGAATGTTTGTCTTCC  
TCCAAATTCATATGTTAAACCTAGCCCCAAATGTGATAATATTTGGAG  
GAAGGCTCTTTGGGAGGCAGAGCCCTCATGAATGGGATTAGTAGCCTTAT  
AAAAGAGACCCCTGAGGGCTCCCTTGTCCTCCACCGTGTAAGGATGCA  
ACAAGAAAGTATGGTCTATGATCCAAAAGCAGACCCCTTGCCAGGTACCC  
AATATGCTGGCACTTGAACCTCCAGCCTCCAGAACTGTGAGAAATAAT  
TTCTATTTTTCATAGCCACCGAGTCTATGGTATTTTGTATAGGAGCAC  
AAACAGACTGATGTGCCACCCCAACCATGATTATACGTGTAATTTATGGTT  
TCTCTGCTAGTAGGGATGCACCATGGGGTAGGAACACGCTTTTCTTAT  
TTCCACACAGTCTTAGCTCTAAGCATGTTCTGAATCAAAGATCCCCA  
TCTTTTATGAATGAAGGAGTCAGTGAATGAATTAATGAAAGAACTGATAA  
CCCTCAATAATTATCCAGCCTTTTATACCTACTATTAACAAGCTTGCA  
TCTACTCCAAATTTATGGGCTTTAACTCTATTTTTGGCCAGCCACATTT  
GACATTCCTGAAGTAAATCTATGCTTCCATCCTAAGTCAAGGAAGGAC  
CTGGACTGTAGGGCCAAGAAAGGTCTAAATCCATGGGTGGGAGAGAGA  
GACTAAATCTGAAAGGAAGAATAGATTGAGCAAAGGTGTAGAGATTGGGG  
AAGGCTGGACATTTGGAGAGAAGGAAAAGGAACTGACACTAAACCAAAC  
AGTCTCACAAACACAATCTCATCCTTCCAAAACCTCTGTGAAGTAAGAATT  
ACTATCCCAGGGCCAGGCACAGTGGCCCATGCCTGTAATCCCAGCACTTT  
GGGAGGCCAAGGTGGGTGGATCACCTGAAGTCAGGAGTTCAAGACCAACC  
TGATCAACATGGTGAAACCCCATCTCTACTAAAAATACAAAATTAGCTGG  
GCATGGTGGTGGGCAAGTGAATCCAGCTACTTGGGAGGCTGAGGCAGG  
AGAATCATTTGAACCTGGGAGGTGGAGGTTGCAGTGAGCAGAGATCGTGC  
CACTGCACTCCAGCCTGGGTGACAGGGAGACTCCGTCTCAAAAAAAAAA  
AACAAAAAAAAAACCAAAAAAAAAACAAAAACAAGAATTACTATCCAG  
TTTTGCAGATGAGGCAATGGAAGCTCTAAAAGTTAAGTAGGAGAAACAA  
ACATGAAATGTATGTCTTATGCTTTTCTCATCCTATTTCTCAGCCTGG  
AATGTCCATTCTCCCTCCACTATGCAAATCTAACTCTTCAAGCTAACACA  
TAGCAATGTCTGAGAAACCGTCCCTGTGTTCACTCTGTTAGCCTCACTTG  
CTCCCTCCCATCCCTCTGTTTCTTTCTGTTATAACACTTCTCTATTCT  
GCTGGCATCACAGTCATCTCCACCTGCCTTCTCACAAGTTAAAGCTTG  
TTAAGGGCAAGTGGTGTCTTTGCCACCTCATTCCCCAGGGCTTCTAACA  
CAGTGCCTCATGCATGACAGAGTTGTAAAACAGGTTACCAAGCTGGCTTC  
AGGCAGGTTTGCACTGGAAGTGTGCTTTACAGGAATACCTGCTCCCCCAG  
GCCCTGGGTCTTCTCTCTGAGTCCAGGCTCAGACTCTCTCATCCTGCTCG  
TTCTCTCTTGGGGAGCCACAGTAACTTTGAGCAACTTTGCATGGGATAGA  
ATGGCCTATTAGGGGCAGCACAAAGACCCCATGGAGGGAAGAGTACAGAA  
AGGGAAAACGATAATCATATTTTTTTAAGATGTGCATTTCTTAACAAAA  
TGCTCTAGTACTTGTCCAGACTTTCAAACCTAAAAACCTAAGCGTCTTT  
TCTTGAAGATCATCAAAGGCCCCAGTGGTCTTCAGGTATGTCAAGCTTT  
CTAGAAAATAAGGTAAGTCATAATCACTTAACACACATGGCTAAATGGC  
CATTTCTTCTAATTTATCAGCAACTGTTACATATTTCTATACTAGAAAA  
AATTTATATTTATACTCAGGGTGGTAAGTTAAATTTGCCATCGAAGTAAA  
GCAGAAAGAGCGTAGCATGTATGTATATGTAACCTCAACTGTGCATGAGAC  
AAAGATGTCTTGAGGAGAATGAGTCTAAGATGCCCTGAGCAATAGTACC  
C

FIG. 3 (52 of 52)

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## &gt;Contig1

GCACCCATGTTTCTAAAGGGCATACCAGCCATAATAACAGGATGGGTGAG  
GATATAGACAGCAGATGACAGAGAGGAGAGTGAAAGCTGGGAATCCCAGC  
TAAAGGCATCAGGTTTATGGAATGAGTAGGGGACAATACTGTGTGTGTTT  
ATACACACATGTATATGTGTGTATATGTATACATGTTTATGTATATATAT  
AATTATATGGTACCATTCTAATTGACAAAATAATCTATCACATTTTACA  
TTATCAGATTTTACATCTATTGTTCTAAATACACTCAGTCATCAGCCCTG  
TGTGTGGGCTCTTACCCATCCCCATGCACACCTCAGCTCAACCACTGATG  
GATGGATCATCTGCCTATCAGAGGTGGCATATTCAGGTGAATCCATGGCC  
ACAGCTGCAGCACTTCCTACCCACGCAGAAAGGCTCCACAAGAGGAGGCA  
CACCCGCTCTGACTGTCCCTAAGCTCCTGACATCTTCACCCCATGAACT  
GCTGCTCCTGGGTGCTTCCCTGCCTTGCCCTGCCACCCCTTGACTGTTCT  
CACCATTGACACAGCTGGTGGCCGATGCAC

## &gt;Contig2

NAAAACGAATCGTCACTATTGAAGCCTGTCTCTCANCGGATCGTGAATAA  
GAACCCCTCCTTGCTTCAAGTTGTCCTGCCTTTCTAGGCAGAGCCACCC  
TACATCTTAAATATATTGATTGATGACTTACGTCTCCCTAAAATATATAA  
AACCAAGCTGTGCTCTTACCAACTTGGGCACATGTGGTCAAGACCTCCTG  
ATGCTCTTGTCATGAGTGGGTGGGTGTTCTCAACCTTGAAAAATAAACT  
TTCTAAATTAACCTGAGACCTGGGTGAGATTTTGGGGTTCACAGCAACAA  
TTTAAAAAACTCACCATTGACCTGAAATTTGACCTTATGCTGTTGCTCA  
CCTCCTCCATGAAAAATAGACGCCATCCTATGAGTTCCCTCAGCCATGTC  
ATGCCACACTTCCAACATGTGTCCCATCCACCATCTGTCTTCTTATTGC  
TGCATCCTACCCAGGCCCTGATCTCTGGACCCATTGTTGTATAATTAAGA  
ATTTGGGGCTGGGCATCGTGGCTGTGGCTCACTCCTGTGATCTCAACATT  
TTGGGAAGGTGTATTAGTCAGGATTCCTCCGAAGGATGCAACCCTAGGGA  
TCCTCTCTATGACCCTATGTCTA

## &gt;Contig3

CGCGTCAACCGACCGATTGCGCGAACCTGCCCATGCCCGAGGACAGTG  
TAATCCTAAAACGTCCCCTGAATCATAAGGATATGAGTGCAGAAAGTACGG  
TTCCCTCTGTCAACACTTTCTAACAACGCTATGTCCGATCCGTGCACTAA  
CCCCGCCCAAGTCACTGAAACACTGATGGGCGCTTCCTCTACAGGTATCC  
AGGGCCAATACCACTACTCCCCCTCCTCCCTGTCCCCCTTCCACTCTCTAG  
AGGCCGCGGATGCCATCCTCTATTAGCACAACCGAAAACGACGGTGAAAG  
TACCACGAAGCTCAGCATCTGATCGGTGCGCCAAATGCGGTTACAACGGCT  
GTCTCCCAACCCCCGTCCCATCCTCCATATTGCCCCCCCCCTATGAGGAT  
GGCCCTATCATCATGACCTCCAAAATTCTGTCTCTCCCGACGTAATGCC  
CCCCCTCGAACGCTGACACCATCAAGTCNGTCACCTCCCAAAATACTCC  
TCCTAATCACCAGGCCGAGTATCCCCGGTTCCACAATACCTCCTTGAGAC  
GGGCCGATATCACACAC

## &gt;Contig4

NGGAGTTTAGGTCAACTAGTAACAAGTGGGATTGCGACTCAGGTCTATC  
TAATCCTCAAACCCACGTCTTGACCCCTACACAGACTGCCCTCCCTCAG  
TCCTCTGTGTGGCCTCAAGAAGGGTCTGGACATTCAAGTTTAAAAATCCA  
TCCAAAGAATCTATGGACCCAGTGGTCTCTGGAGTCAATGTTCTGAGGCT  
CAGAAGGGCCAGGCAGGAGGGAGCCGCTCTACACAGTCTTGAGCAGAGT  
GGGCTGTGTCCCGGCACAGCAGGGGAGATCATAACAGAATTCTGCCCTG  
GGCCCTATTAAAGTAGGACCTTTAGGCTGCCGGTGTATGACCACAGGTC  
CCANGTCTGCACGATTGGCTGTGTGTGGAATACTTCACTCCTTGCGGCC  
TTGTCTTTGGCAGAGAGCACCGCTGCTTCTCTGATGGCCACCAGGGGGA  
GGCGCTCCCTGGGAACGGTTTGAANGGGAGCCTCACCCACACGTGCCT  
TCCGTGGTACCCAGCACCAGCTGCTACCCATGGTTACCCACAGGCCCAGC  
TCTGCTCTGAAGAAGGAGGAGTGGTGGCGATCANGCCTTGTCTGCATCCC  
GTGGCTGCCCTTTCTTTTCTTT

## &gt;Contig5

GGGAGCTAACCGCTCACTGGGATTACAGGTACGCACCACACGCCTGGCT  
AATTTGTATTTTAGTAGAGACGGGGTTTCTCCGTGTTGGTAAGGCTGG  
TCTCGAATCCCCAACCTCAGTTGATCTGCCCGCCTCAGCCTCCCAAAGTG  
CTGGGATAACAGGTGTGAGCTACCATGCCTGGGCTTATATGTTTCTAGTC  
CAACATTTAGCTACCTTTTTTTTTTTTTTGGAGACGAAGTCTCACTCTGT

FIG. 4 (1 of 61)

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TGCCCCAAGCTGGAGCACAGTGGCACAATCGTGGCTCGCTGCAGCCTCAAC  
CTCCTCAGGCTCAGGTGATTCTCCACCTCGGCCTCCCTAGTAGCTGGGA  
CTACAGGTACGCACCACTACACCCTGCTAATTTTTTTGTTTTGTATTTT  
TTGTACAGATGGGGTTTCTTCATGTTACCCANGCTGGTCTTGAACCTCTG  
GGCTCAAGCAATCTGCCTACTTCAGCCTCCCAAAGTGCTAGGATTACAAG  
CATAAGCCACCATAACCCGGCCTACCTACTTTTAACTTGTGGAATTTTCTA  
TAAGGTCANGGATGCCTGNGGGAAACAAAAGTTTCTCCCTTGGTATATGCA  
AGTAAATCCACATGCTGCCTCCC

>Contig6

AGGACTGTAGCTGTTGTCTAGTCACCAGGCTGGACTGCTTGGCATGATCT  
CAGCTCACTACAACCTCCACCTCCTGGGTTCAAGGGATTCTCCTGCTTCA  
GCCTTCCAAGTAGCTGGGATTACAGGCATGCACTACCATGCCCCGGCTAAT  
TTTGTATTCTTAGTAGAGACGGGGTTTCGCCATGTTGGCCAGGCTGCTCT  
CAAACCTCCTGCCCTCAAGTGATCTGCCTGCCTCGGCCTCCCAAAGTGCTG  
GGATTACAGGCGGTGAGCCCCCGGCCACATGTAAAGTTTATATCTCTGT  
TGTTTACCTTGTTTTGACCTAGTCTTTTCAGTGATTTGAATCTTGATTCT  
AGTCTTTTGTATTTTAGTGGTACTTCCAGCTTTGTGTCTCTGTGGAT  
GACATATGAGTCTTGCTTCTTCATGCCAATTTAAGAAGACTGAACGGGAA  
TAGGTCAAAGGCATGGCCATGAGCGATTTCTCTCCAGCTTTTCATGGTGT  
TCAGCTTCAAATCTATTCACATATTGGACCTGCAAGCCATCATCTTATCC  
ACAGGCTATCATCATAGGTGAATGTAAATTGGGTTTAGGTGGCCAAAGCTG  
AACGTGAGATATNTTC

>Contig7

AGCATGTTCTCTAAAGGCCTATCAAAGCTGACATCAAAGGGATAAGTTCC  
AGTTACCCAGCTGAAGGGAAGGAGGGTGTTCAGATAGAGGAAGGATAAG  
CATGACCTATTCAAGGCCAGTGAAAGAAGCGTGCAACGGCCAAGTCAGGA  
GAACCTGAAATTGTGTCAAAGAGCTTGGATGCAAAGAGCCGTGGGAGACT  
ATTGGGGGTTTAAAGCAGGGATATAATATTCATTCAAGCATGCAGTAAAA  
GGTCACTGGCACCTGCCATGGGCCAGGACTCGGGCTCTACATGATTGCGT  
CTGTTTGGAAATATCACCTGGCTGTGAGATGAAGAACAGGTAGGAGGG  
TCACAAAACCTGAAGCAGAGAGACTGTTGAGGAAGTAAGCTGTTTTGTG  
TGGACTGTGGCAATCACAGAGGCAGAGGATATAAATGCACAGAGACACAA  
GGCATGTGGGAGGCAGAAGGAATCAAATACAATGAGTGATCAGATGTGGG  
GTTAGAATGGTGAGTGANAAAGACATACTCAAGGTGACACGCCAGGTAT  
CTGGGTGGATGGTAAGACATTATGGAAGTAGAATCGAAGAGGAGGTGGGG  
ATGGACATTCTTCCGTTTAGAGGGGTTACCAGGAGGATTTGCCGGAAC  
ATGGAGAGGATTAACCAGGAATCCGGTGCCTTTTCCAAACTGGGTGGA  
GGG

>Contig8

GGTGAATGCTTTGGCACGCTGTGTAGATTTTAGGTGACGGGTGGTGACAA  
TGAGTCCGTGTCGAGCGCTGATTTTTCGGCCTTTAGAGCGAGATTTATA  
CAATAGAATTTGGCATGAGATTGGATTGCTTTTAGTCAGCCTCTTATAGC  
CTAAAGTCTTTGAGTGACTAGATGACATATCATGTAAGTTGCTGATAGGT  
TTCCAGTTTTCCGCTCCTAGGTCTGCATATTGTACTTTTCTCTTACTCG  
ACTTAACCACTACCAACCCAGCTTCTCAACGGATTTATACCATGGCACTT  
TAAAGCCAGCATCACTGACAATGAGCGGTGTGGTGTACTCGGTAGAATG  
CTCGCAAGGTCTGGCTAAAATTGGTCATGAGCTTTCTTTGAACATTGCTCT  
GAAAACGGGAACGCTTTCTCATAAAGAGTAACAGAACGACCGTGATGTC  
GAATGAAGCTCGCCATAACCATAAGTCGTTTTTGTCTCCGAATATCAGACC  
AGTCAACAAGTGTCAATGGGCTCGTATTGCCCGAACAGATTAAGCTAGCA  
TGCCAACGGGATAAACGAGTCGCTCTTGGTGGAGGG

>Contig9

GGGGTGGGGCGCCTGGTGTCTTCTAAAGAGGATCTCCTGCCAGAAATGGTG  
TGCTGACACTGTTGTCCTCCTTGGTGTGGAACCTTGGTGGGAAGAAAGGT  
TGGAAGGGGAAATTTGATCCTTGGATTTAACCCGAGTTTGTACTGATG  
CTCACAAGACTAGGGGAAGGATAAAGGCAGGTGAGTCACTCTAGGATGGC  
TCANTGAGCTCCACAGAGCTGGAACCACAGGCACCAGGAGGGATTAGAG  
CAGGCCTCAGTGACCTCAGCTGAGTGAACCAATGAGCAGGTGATGGGTC  
CAGGCAGAGCCCTGTCTCTTTAGGCAAAAACCTTGAAACACCGTTCCC  
ATCCTAGCCTGTGTTCCACCCAAAGCTGGCCAGTCTCCAGGCCCTGCCTG

FIG. 4 (2 of 61)

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AGCCCCAAGGAAGTGGTATGGTGAACAGAAGGGCCATTCTGTCCAATG  
TGTGAGGAACCTTCATTTCAGACTTGTGGGAAGCCCTGATGTTCAAAAACC  
TCAATGATATCATTCAATTTCCCATCCATTCAATGCCCATCCAATGCCC  
ATCCGTTCAATGCCCTTCCATTCTCTTCAGGGAAATGAAAATTGTTCA  
GAAATCCTTTCTCTTCGAGAAACCAACCAACCAAAACCGCGAAATTCA  
CTAAACTAGCCAAGACACAATCCTGGGTTATTTTCTTTTCCAAACCTC  
CTGTGTTTAAATTAATTCCTACCCTGGTTCTCGGCCCTTACTGCGAAGGTG  
AACTCACCTAACCTCTCCCAAACAGAGAAGAACTTCTCTTGGTAAAAATG  
GGTTTTAACACTTCTAAAAAACCCCC

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GCTATGGTTCTAAAGGTAATGGACTATGGCGTACACAACGTCTCGCTCAT  
CGTCTGCCAGGAGGCTAAGGTATCCACGGACAATCGCTGAGCAACAGTGT  
CGTTGATCCATCTCTGTACGCACTTGTCAACATGGCAGGAGTACGGGAGC  
TGCGAGAATCCTCTCTGTGATGTCCACGGAGCATGCCGTGAGACAACG  
CCACGAACGGCCCTCGGAGANANCTACTCTGCAATGAAGACGTACGATAC  
ACACGTAGGAGTCTTAGCTCACCAGCCGTATCTAGGTATACTGTACTCGC  
GGATACTCACTCGTGCAATGCGGCAATAGATCGATACGCAGTCGTACGCC  
CATGCTCTCAGTGTGTGACCTTCTGGCGGTAGCGTNGTGGGCGCTATTAC  
TGTGCGCAGCAGGCGCNTCGTACATGTGTGCGGTAGCGATGCCAGGAGCT  
GTAACATAGCAAGTCGCCCCCTACTCCTATCACTATCCCTACGCTGGAC  
CGCACTCGAGATCTGAACGCACGTCTTAACCTGCCAGTACTCGTGAGACC  
TATACTGCGCAAGCCTTGGCTAGGAGATCCTGCAGCGCCGGCAAAGAATC  
AGCTATGATCCCCTTGGCATTATCGCACACGCACCATAGAGTATGTGCAT  
ATTAACCTCTGAATGTGCTGCAAGCAGACGGTTGCTCAACATATATATGG  
ATGTGGGGAAATCGCCCTGGTCAACGCCACTTGGCGTCAGGAGGCACCAG  
CACGTCTGAGTGTACGCACGTTACTC

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GGCCGAATGGTGAATTCATCCGTCTGAGGGGGTGAAAGACGGGGAG  
TTATGCTGTAATGGCACCCTCACCCCTGGGCTTATGAGCAGACCTAACCC  
TCCANAGTGTCTGGGATTACAGGCATGAGCCACCGTGCCCGGCCAGTAT  
CTGAACCTCTGTGGCCAGGCAAAAAGTCTGTGTTACTCGTCTCCTTT  
ATCATTCAATGTCCATATTCTCCCATTTGCTAACATTTATGTTTCTGCTCC  
ACTGGATTCTTTGGATTTTTCTAGAACATAACCCATGCTTTGCATTGCCTT  
GGTCTTTGAATATTTGGTCCACTTTTCTGCAAAGTCCCCTCTCACCTTA  
TCTTCCTGGTAAACTTCCAGCCAACACCTCTTACTAACAGAGAAACAT  
GGTCAACTGTGCACAGGCTTGCACAGAACTGTTCTCATATTGTCTTGT  
CATTGTCAATGTGGCAGAGATGCACCTTAGATACCTCTTTGAGAAAGGAC  
TCACTGCCCGAGTGGCTGGCAGTGATGAGCTGATAGCTCCAGCTATAGA  
CTCCTTTAGGGTCAACCTCTGCTTCCAGTTGAGATCATATCCTTTGCAG  
GGTGGCCTCCCGAGTGATGACTAAGGCAGTGTTACAATGGCCTAGTCATT  
TCCTCCCAATGCTGGACTCCCAATGAACCATCTGCTCCGGAGCTTCCCAC  
TGGGCAGTCAGAGACCTTAGCTAGTCTGCCTCCGAATCAGAAGGCTCTCT  
CTTGCCACTCTGGCC

>Contig12

GCTGTGTCTAAAGATTACGGCTGTAGTTCCTCAACTCCCGCCGCCCTCTAC  
TGTGTCTCTTAATGGCAGTCATTACCATCTTCTGTCCCTCCCCTTCA  
TTTCTTGGATGGTGAATGTCACTTTGCTGCAACAGAACCCTGTCCCAATC  
CTTGATGGTTCAATACACACATAGACATTCTTTTAAACAGGGCGGCCTCT  
CAGGTCTTTAATTTTCTTCCCTCCAATAACCTTGTGATGATCCCCAGCT  
TAGCCACTTACTGCCAGATCATTACCAGTAACTCCAGCCCCCTCTTAATT  
CTAGTTTCTAATATCCTAATCTGTGACCTCACATTCCAATTCTTCATT  
TTATCCCCTGAGTCAAAAAATCCTTTGATCCATGCAATCCATTAAGTCAT  
CTACCTTTTCAACATCTTCGCCCCACTAGGGTTCTCATTCTTTATTAC  
CCATATGAAATTCCAAGGCCTGTTGGAATCACTCCCTTGCAGCCACTGTC  
AATACTTCTGCCCTTTTACTTCATCACCTTATGTGGCAAACACACAGC  
CCTGGTGGAGTCGATCCTTACCCCTGCTCTGTGCCAACAGCCGCACACGC  
ATGGCTGATGGAGGTTGGAAAAATCCACACATGCAGTGGGCCCCGTATGT  
CCATATACGTATCCAACCTCCAGCCTTGCATATGCCTCAGTGTGCTGCTGA  
CAACACATTATATGTTTTCTTAGTTCTTTCAGTCTCCTGGGTGCCTAGG  
TGAGTATCTCAGACATCCTTCTCTCTCTGCAAAGCTCCAACACCTCCACG

TCACATTCAACTGATGACGTGTCTCCTATGTCACTTAGATCACAGAGGC  
ATACATAAACAAATCCCAGCCACTGCCAGCACTCTGCACATCTGCGAGCA  
TGGCACCCCCAATCTAGGCCTTTCCTGCTGTCACTTGGGGTGAGCTGATT  
ATACTCGATCCTAGTCATTTCTACTTATGCAC

>Contig13

CTTAAGGCCCTCCCTCTAACATTTTAAATTTAAGATTGAAAAAGCAAAGATT  
ATTCTGTTTTGGCTGCGCTATAGTAAAGTAACCCCTATGNCAAATTTTG  
ACACCTTATAGTATTTGACAGGGATAAGTATAAAATTGCTTGATTGATAC  
ATCCACACCCAAATGTATGCTGGGAATGATTTTGTTCACGGCACTCATT  
ACTTAATTTTAAAACTCTTATTTAAATTTGCAATGTTTTAAATGACCAT  
CACTTAAAGTAGTAATCAACAGAGGTTAGGAGAACATAACAATACTCTTT  
CTCTTAGAAAAATACAACAGAAATATAATTTTTTACAGTTTTGCTCCCAAA  
CTTTTCTCTGTAATAACATGCCCTTACTCACCTTTACAATAGGTTTGTGT  
GAGAATCTTTGTAATGTAAACCCCTGGGTGTTCTGTGAAGCATTTTTAACT  
TCTAGTTTACACTGACTCTTATTCAAGTGTTTTTAAAAATATATTTAAAA  
AACTGGCCAGGTGCAGTGGCTCACACCTGTAATCCCAGCACTTTGGGAGG  
CCAAGGCGGGCAGATCACAAGGTGAGGAGTTTGAGACCAGCCTAGCCAAC  
ATAGTAAACCTCGTCTCTACTAAAAATACAAAAATTAGCTGGGCGTGGT  
GGCGGGCGCCTGTAGTCCCAGCTACTCAGGAGGCTGAGGCAGAAGAATCG  
CTTGAACCCGGGAGGCAGAGTTGTGGTGAACCAAGTTTGGCCCAATGCA  
CTGCCAGCCTCTGCAGNGACAGCC

>Contig14

GGGGGCGGGCCGAGTGATCCTAAAGCCCGCTCGCTTCAACAACAAAGCCTA  
ACAGTCCAATCACTTAATGCTGCATTTATTCTGGGGAAGCAAGTCTCCT  
TTGCACTTTACACAGTGAGATAATCAGTTTCTCATGTGGACCACTGGGCC  
AGGAGGGCCTGACAAAGGGCAGTCTACATTTGAGACTGGAACTGCTCCC  
AGAACTATTTCTTTCTAGTTCCACCTCGGTCTGAGGTGCCTGAGGAGAG  
GGACTCAACAGAGGAAGCAGGAGCATAGCTCAAAGTCTCAGAATGGA  
GAGGAAAAAGATCCTCACAAGATTACGTAACCTACAGGCGTGTGCTGCT  
TCAGTAGAAGTTTCTCTCCCTCAATCCTGTACACTTTTCCATACATTAC  
ATACTCAAAGTGGTCAGCCCTATGGAGCAATAGCAGCAAAGTTATTCTTA  
ACAGTAATTAACAATATAAAAGATCCCATTTAAAAATGGTTACTGGTCAG  
CCGGGCGTGGTNNNTCNANCCTNTAACCCCANCACTTTGGAAAGCATGCG  
GGCGATCCCAAGTCTGATATCGAAACATCTGCCTAACATGTGCAACCCCT  
CTCTACAAAATACAAAAATATCCGGGCTTGTGTTGGCGCCGTTATCTCA  
CTACCCGGAGCTAAGTAAGAAATGCTTTACCTGGAAGCGATTTTTTTACT  
TATATCCCCTCTCTTACCAGGGCGGACCAAATCTTTAGTATAGGAAAG  
TTTATTGTTTTATGCCTTTGTCAAGGCTCTACTGTATCTTTTCTGTCCAC  
TCAC

>Contig15

GTTTCTGAACAACAGCAGGCGATTCTAGCCCTGTACCCGGGGCATTGTG  
CAACACTCGACAGGCTGAATTCGTCCATAACGGTGTGCCCTCTGGGAT  
ATAGGATGAAATGAATTGATCTGAGTACCTGGGATGTAAAGTTACTAAAA  
CGCCAGCTAGGTTACGCCCCGATGCTTAAATATGATCGTGGCCTACACC  
TCGTCCAGCAGAAAAAGTACCCTTTCTTCAACACCACCTCACGATCCTCC  
AATTTAGGAGCTATAAACTCATGACTCTTTATTTACCCCTGCAGATTCT  
TCAATCCAATAGTGTGTGTCTCCCTGTGAACCTCACGGATATACCGATTTT  
CCCCACGTCAATTCACACGTCGCAATCGCTTAGTCATCCCTATGTATGA  
GAATCATGGATGACTATGTTGAAGTCCATCTATAAAGTTCAACCCCCATC  
TCCGTCCCTGATTCCCCCTCCCCAAGATCACCAACGCGACTCGACATATT  
GTTATCGCCCCAAGGGACCTCTTGCATCCCCCATATCCACTGGTCACCTCC  
CCTCTTGGCTGGAAGTCACCGGAAGTTCTCCACATGTTGT

>Contig16

TGCGAGCGATGTTCTTAACTTTAGCGCCATTGACTCGAGCATGGTCATG  
GCTGTTTCCTG

>Contig17

AGGGTGTTCTTAAAGGATACTACGTTCCCTAAAGTCCAGAGAAAAA  
AAAGTAACATAATGTGGCTTATTTGGTATAAAAAATTTACAGGAAGCATT  
GTCAAATATGAAATAGTGTGTTTGGTTTGGTGGGCTGATTTGTATAAAT  
ATGTTATTGGTATGTGTTCCAAAATTATAGGAACTCCTATAATTCTGAT

FIG. 4 (4 of 61)

58/118

ATGACTTGGTGTACATTATCAGTAATAATTATAATTGTTATGGTAAATTA  
TTGTGTGCCATGGAGGTAAACAAATTTCTCATCAAGTGTGTCTTTGACTA  
TGGTTGCCCTAAACTTTTTGCCATTACAGACAATTGTCTTGCTTTGGT  
CCTCTTTAGAAGGTGGTTTTATAATCAGCTATAAACTCTAACGGGTGCT  
CTTGAAATGCAGGCTTAAGATAGCTTTGGAGACTGTGACATCAGAATAGAG  
GAAAACTTTCAGTATTCATGGAGTGCTGAAATATTCATGAATATCAAGC  
AAAACAGGAATTAACCTCATAGATGGAATAAAAGAATGCTGAAGTAATC  
TTTTTGACTTTTTTTCTTAAATGTTGATCCTTCGTTTTGTTTTTCAGAG  
TCAAGGAAATTTTTCTGTTGAGATATTGACAGCTTTTAAACAATTAAGTAT  
ACTCCAGTGAACACAATTTGGAGCATATTTGTGTCTCTCTATATATATTT  
GGAAACAATNTTTGAGTATTCTTAACCTATTGCAATATT

>Contig18

GGTTGTCTGTATACCAGTAATGGGATTGCTGGGTCAAATGGTATTTCTG  
GTTCCAGATCCTTGAGGAATTGCCCACTGTCTTCCACAATGGTTGAACT  
AATGACACTCCCACCAAGCTGTAAAGCATTCTATTTCTCCACATCC  
TCTCCAGCATCTGTTGTTTCTGACTTTTTAAATAATCGCCATTCTAATCG  
GCATGAGATGGTATCTCATTGTGGTTTCAATTTGCATTTCTCTAATGACC  
AGTGATGATGAGCTTTTTTTCATGTTTGTGGCCACATAAATGTCTTCTT  
CTGAGATGTGTCTGTTTCATATCTTTTGCCCACTTTTTGATGGGTTTTTTT  
TTCTTGCAATTTGTTTAAATTCCTTGATAGATTCTGGATATTAGCCCTTT  
GTCAGATGGATAGATTGAAAAAATTTCTCCTATTCTGTAGGTTGCCTGT  
TCACTCTGACAATAGTTTCTTTTGCTGTGCAGAAGCTTTTCAGTTTAATT  
AGATCCCATTGTCAATTGGCTTTTGTGCAATTGCTTTTGGTGTCTTAA  
TCATGAAGTCTTTGCTCATGCCTATGTCCTGAATGGTATTGCCTAGGTTT  
TCTTCTATGGTTTTTATGGTTTTAGGTCTTATGTTTAAATCCTTCTTTTT  
TTTTTTTTTTTTTTTTGAGATGGAGTCTTAGTCTGTTGCCCAGGCTGGA  
GAGCGAGTGGCGTGTCTNTAGGACGC

>Contig19

GCATGTTGTCTAAAGGTTTGTCTTCTCCTCCAAATTCATATGTTAAACCT  
AGCCCCAAATGTGATAATTTGGAGGAAGGCTCTTTGGGAGGCAGAGCC  
CTCATGAATGGGATTAGTAGCCTTATAAAAGAGACCCCTGAGGGCTCCCT  
TGTCCCCTCCACCGTGAAGGATGCAACAAGAAAGTATGGTCTATGATCC  
AAAAAGCAGACCCCTTGCCAGGTACCCAATATGCTGGCACTTGAACCTCCC  
AGCCTCCAGAACTGTGAGAAATAAATTTCTATTTTTTCATAAGCCACCGAG  
TCTATGGTATTTTGTATAGGAGCACAAACAGACTGATGTGCCACCCCAAC  
CATGATTATACGTGTAATTTATGGTTTCTCTGCTAGTAGGGATGCACCAT  
GGGGTTAGGAACCAACGCTTTCTTATTTCCACACAGTCTTAGCTCTAA  
GCATGTTTCTGAATCAAAGATCCCCATCTTTTATGAATGAAGGAGTCAGT  
GAATGAATTAATGAAAGAACTGATAACCCTCAATAATTATTCAGCCTTT  
TATACCTACTATTAA

>Contig20

ACGGTCTCTAAAGACTTTCAAGAGCTGGATTTTATGCTTTAGGTGAAGG  
TGATAAAGTAAAGTGCTTTCACTGTGGAGGGGGCTAACTGATTGGAAGC  
CCAGCGAAGACCCCTTGGGAACAACATGATAAATGGCATCCAGGGTGTA  
TATCTGTTAGAACAGAGACACGAAATATATAAACAATATTCATTTATC  
CCATTCACTTGAGGAGTGTCTGGTAAGAACTGCTGAAAAAACGCCATCAC  
TAACTAGAAAAATTGATACCATCTTCCATAATCCTATGGTACAAGAAGCT  
ATATGAATGGGGTTCAGTTTCAAAGACATTAAGAAAAATAATGGAGGAAAA  
AATTCAGACATCTGGGAGCAACTGTAAATCACTTGAGGTTCTGATTGCAG  
ATCCAGTGAAGGCTCAGAAAGACAGTACACAAGACGAATCAAGTCAGACT  
TCATTGCAGAAAGAGATTAGTACTGAAGAGCAGCTAAGACACCTGCAAGA  
GGAGAGCTTTTGCAAAATCTGTATGGATAGAAATATTGCTGTCTTTTTTA  
TTCCTTGTGGACATCCAGTCACTCGTAAACAATGTGCTGAAGTGGTTGAC  
AAATGTCTCAAGTGGTACGCAGTCATTACTTTCAAGCAAAAAAATTTTAT  
GTCTTAATCTAACGCTATAGTAGGCATATTATGTTCTGATTATCCTGATT  
GAATGTGTGATGTGAAGTGAATTAAGTAATCAGGATTGAATTCCATTAG  
CATTTGGTACCAAGTAGGAAAAAATGTAAAGCCAGTGCTTAGACACA  
GC

>Contig21

CGCTGTCTTAAGAACTGGGCTAGGAGTGAGCAGTGAGCCAAGATCGCACC

ATTGCACTTCAGCCTGGGCAACAAGAGCAAACTCCATCTCAAAAAAATA  
CATATATATATATGACCCATAAAAAAGGAGATAAATCAACACTTCAGAAGT  
GACCCAACTTGCAAAGATACTATAATTAACAGAAAAGGACAGTTTACTA  
AGTACTCCGTATGTTCAACAAGTGAAAGATTAAACATATTAAGTAGAGAT  
GTAGAAGATATAAGAAGATCCAAAATGAACTTTTAGAGTTGAAAACCTACA  
ATATTTAAGATAAAAAATACACTAGGTGGGATTAAAAGTAGATTACACATT  
GCATAAGATAAAAAAAATGAGCCTGAATACAGCACAGTATAAACTATCT  
TAAACAAAAACACAGAGAGAAAAAATAACTTTAGAGACTTAGCTCTTATC  
CTCTATTGTTTTCTAAACAGAGGATAAGGGGCAGAAAAAATGTTTGAAGA  
AATCATGATTTTTTAAATTTCCAACCTGAGATAGGAATAGCACTGGGTAGTC  
ACAGGAGGCTGGAAAGACCCAAACAGCAGTTAAAACAGGAACTAGGCAAA  
GAAACCAAAGGATAACAGTAAACCTAAACTAAGGGAGAGAAAACTGACAA  
AAGCTGACTTAGGATAACTGAC

>Contig22

CCTGAATATAAGCCGCAAGTAACCAATTAATTTGTTTTCCAAAATTGTA  
TTAACAATCTATGAAATTTTTATCTTGACCATAGCTATAACTCCAGAAG  
CCTTTTATAACCTCTATAACCTTTATTAAGGAGTAGGTTAATGCTTCAAG  
AAAACCTTGTTAATCTGACACAGGACCCATATGCTGATCTTGCATCAGTG  
TGGCTTGACATCAATGATTATGATTAAATTTATAGAGAAATTGAACCTAT  
TTTATCTCTCAAAATTGGCCCTTACAATCTCACACACCCACCTCTTCCAC  
TATAGTTCCTGGGCCTTGAGTTGAATAGCTTTAATTTCTGGCTCTGTGTT  
TCAAGAATGCAGTTTATTTTGATTGGCATTCTTACCAGTCTGAAGATG  
AACCTTTAATTGCTGTCAGTATTTAAGATTTAGCAGGACTTGTCTTTTA  
AGAACCAGGAGTCAAGCCCTATAACTCAATGTCAAGGACTTTAAAAGC  
ACATACATAAAGATATATGGATGTAATAATCATAATTTTTAAAAAATTGT  
ATTAATCTCAGTGTTTTCTAAGCAAACCAAACTTAATAATAATGGCATA  
GAAATTATTTCAATAAAACATAAAATCTGTTAAGCCAGTTACCAAAGGC  
AAAAGAAAAGACCTTCTGCAATGCACAGAAATATTATGTTGGAAGAAAACA  
TTTCCTTTAGACCTTTAAGAAAACATTGTTAGCATCAGGACACAACAAAC  
AGAATCTGAGGGTAAAAAACGTATATGAGCTGAAGGGAGTTGAAGGAGGG  
CATTACTATTTCCACCTTTTAAAGGGGAGAGAAAACCTAAAACAGCAA  
GATGCAATAAAAGCTGAACCTTGGGTTAAAAAAAATTCTTAAGTCTCTT  
ATAATTTATTAAGAGTGAATCAACCCCGTAAGAAAATTTCAATGTTCTAA  
CCAATTTTTTAATATATAAGTAGTTTTTTAACATCAACCCAATCTCTAGA  
AAGACCATTATAATTTCCCTTTAATTATAGACAACCTTTATCATATAAAG  
TTTTTTTAAATAAATCCTCTATTGTGACTTACACAGACTATTCATGACA  
TGCTTGAGACTTTCTGGTTTGTCTGTAACATCCTTTTCTTTCTTTCTT  
TTTTTAAATTTTACTTTTACGTTCTGGGATACATGTGAAGAACATGGAGGT  
TTATTACGTAGGTGTACATGTGCCATGGTGGTTTGTGTCACCCATTAAAC  
CGTCATCTATATTAGGTATTTTCTTAATGTTATCCCTCCCTTGGCCCC  
CACCTCCTGACAGGCCCTGGTGTGGGACATCCCCTCCCTGTGTCCATGTG  
TTCTCAATGTTCACTCCCACTTATGATTGAGAACTGCAGTGTTTGGTTTT  
CTGTTT

>Contig23

GCTAAATATAAGCTATGATAAAACAGTTGGCCCTCTGTATCATGGGTTTC  
ACAACCTGTGGATTCAACTAACTGTGGATGAAAAATACTGGGAAAAAAG  
AATGGCTGCATCTGTACTGCACAAGTGCCTGCTTTATCTCGTCATTAT  
TCCCTAAGCAATACAATATAACAACCTATTTATATAGCATTACGCTGTAT  
TAGGTATTATAAGTAATCTAGAGATGATTGAAGTATACAGGAGGATGTG  
CTTAGGTTACATGCAATATTATGCCACTTTATATAAGGCCCTTGAGCCT  
CCTCAGATTTTGGTATCCATGGCAGTCTGGAGTCAATTCTCCTGCAACA  
TCTCCATTTGTTTCAGATTCTCTTCTATATCATGTTTATATCAGAAAATCT  
ACATAAGATTTTTTAAATGTGTTTATATAGGTTTTGTGTATTTTTGGTTGT  
TAATCCCTAGATATATGCAGTATTTATTGCTATTATGAGTAGTGTCTT  
TACCATGTATTCTAGTTGGTTATTGCTGACAGAGAAATGTTGCTGGTGT  
TCTAAGTTACCTTGTTTCTAACCAACCTTGCTGAACCTTATTAGTTCTCA  
TAGTTTTTAATTAATCTTTCTTAGTTCTGATAACATAATCTGCAATAAT  
GACAATTTTATATCTTTCTTTCCAATGCTTATATCTCTCAGTCTCTTTA  
TCCCAAAGTATTTTCCAGGATCTCCACTATAACATTAATAGTAATAAGA  
ATTTCTGTCTTGTACTGATCTTAAGGAGAATAAATTTAAATTTCTCTG

FIG. 4 (6 of 61)

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TCAGGTTTTATGCTTGATATAGATTTGTGATATATAGCCTTTCACAGGT  
AAAAAAAAAATGCTTTCCTAGTAGTCCTAATTTTTTAAAAAATCATCATA  
AATAGATGTTGAACATTATCAAATGCTTTTTCTGCATCTATAGAGATAAT  
CATATGGTTTTTACTATTTATTAATGTAATGAATTAGACCAATTTTCTA  
ATGCCAACTCTTCTTGTATTTGTAGGGTAAATCCTATGGGATCATAAAA  
TACTTTTAATACATTGTTAGATTTGAAGAGTTAACGCCTTATTTAGAACG  
TTTTCAAGTCACATCCATAAGTGAAATGGCACTATAGTGTCTATTACTATT  
ATATTTTTCTGGTCTGAAACCAAATTATACTCACCTCATACAGTAAGT  
TGGGCAACTTTTGTCTTTTTTCTGAAACAATTTGTGTATAGAAGAAAT  
TAACTGTTCTTGAAAGTTTGATAATAATCATCCAGAAAATTATCCCCAT  
CTAGGGCTTTTACAAAAGGAGACTCTAGAATGCCATTTCTGGTTTCTTG  
ATGTGTATTGGCCTCTTTCATTTAGGCTTTTGGATTTTTTAGGGCATT  
TTCATATAGGCTTTTTACCGG

>Contig24

CATAAACTTCAGGTTGGATGTTTCGGTCAAAGTGGTCCGGCGATGCGAAAA  
CGAGAGGGCTCGAGGACTGGGCAGAGAACTATTTGAAGGTATCTCTCAGG  
GGAAACCAAGCGGAAGGCGGGGAGTAAATTTGGGAGGGAGCGACGGCCTT  
CAAAGAAGGGGCTTGCAATTAGATCGGCGAGATCCGGGAGGGTCTGGTGGG  
GAGAAATGACTAGAGGACAAATCTAATGGAGAGACAGACGGAGATAGATA  
TCGTGACAGAGAGAGGGACAGTGACAGCGCACAAACAGTGCAGGGTCCATG  
AGTACAAGGCCCTTAAAGTGTACACCCCGAGCCGGAGTCATGGCAATTCGAT  
TCCTGTACTGACCAACCCAGGATTTGGGTAGACTGTACGAGTTAATGAGCA  
TGGTCCCCAACAAGACTGCTTCGACCTCAGATGCAAAGCACACTTCAGGG  
GTCCCCAAGCCACTCATGTTTTTTGAATGACTGCCATAAGTTCAAAAATT  
CCCACAATTTCTCTCAGATTCAATAACTGGGTATAACCACTCATAGAATC  
AAGAAAATGCTATCATTATTATTACAATTTTATTATAAAGGATACAAATC  
AGAAGGACTAGCCAAATGAGGAGACACATAGAGAGAGGACTAGTAAAAAA  
CAGAGCTTCTGCGTCTTACCTTCAAGGAATCAGGATGCACCACCCTCCA  
GCACATCAAGTCTCATCAACCAGGAAGTTCCTCTGAGCTCCAATGTCCA  
GAGATTTTAGGGAGGATTCAATACATAGGTATCATTGATTAAATCATTGG  
CCATGTACTTGAATCAATCTCCAGTGTCCCTCTTCTCCCTAGAGGTCTG  
AAGGGTTGGCTAATATCATGTGGCTCAAAGCCCCAACTCTAATTACCTTT  
TTGGTCTTTTCAGGGACTAGACCCCATCCTGAAGCTATCTACAGGCCCTG  
CCATGAGTTAGCTCATTAAACATAACAAAGACACTTATATTACTCAGAAAA  
TTCCAACAGTTTTAGAACTCCATGTGAGGAACCTGGGACATAGATCAAA  
TTCTTPTTTTTTTTTTTTTTGGAGACAGGGTCTTGCTGTGTTGCCAG  
GCTAGAGTGCAACGACAGATCACAGCTCAATGCAGCTTCAACTTCCCAGG  
CTTAAGTGACCTTTCCACCTTAACCTTCCAAGTATCTGGGACCACAGAAA  
ATGGCTAATTATCCTGGCTGATTTTTAAACTTTTTTTTTTTGTAGGGATG  
GGATCGCCCTGTGTTGCCAAGGTTGGTCTCAAACCTCCTGGGTCAAGCAA  
TCATTCTGCCCTGGCCTCTGTGATGGTTAATACTGAGTGTCAACTTGATT  
GGATTGAAGGATACAAAATAATTTTTGGGTGTGTCTGTGAAGGTTTCG  
CCAAAAGACATTACTTTGAGTCAGTGGACGGGGAAATCCCCCTTCCCCA  
TGGGACGGGGAGACCCCCCTCCATCCAGGTAAAAAATCTAATCACCTGC  
AATGTGGCAGAAATAAAGGAGGGAAAAAACGGGGACCCCTANATGGGTTA  
TTCTCCACCTAATTCTTCCCCCAGG

>Contig25

CCATGTATTTCAATTTCTACAGACCCTGAGATGAATTTGTCAATTGCCACGG  
GGTCTGAAGTTCAAATACTCTATTTGGTATCCTGCCCTGTGGTTAACT  
GTGATCAATTTCACTCACCTTGTTTATGATGAGAGGTGCCACCATCTGGCC  
TCCTCCACTCTGCAATCCTGTTAATTCCTATCAAAGCTGAAAACCTGCTG  
CAGCAACCCACACCATCACCTCCAGCCTAGAGAGGGAAGCTACCAGTGAGC  
TCTCCTGGATGCCGGTGTGCCCTCGCCAATACATTTCTTCTAGTCCCT  
TGGTCATCCTGAGGTGTGTGATTAATGGACAGCTATGTGGATTGCACATA  
ATAGATGTACTCCAGCATCTTCATCCCTGATTTTCTTTACAGAAATCAC  
TCAACCTTAGCAACATGTGAAAATCACCTAAGGACATTCTTTAAATCCCT  
CTGTCCACATGGCAAACACAAACCACTTAAATAAGAATCTCCAGGGAGTCA  
CTCAAGCATCAATGTTTTTTAAAGCTCCAATTTAAGGATCATTACATTA  
TGTGGAAGAAATTATAGTATTTTCAAGCTTACTGACTGTAAACCACCACCA  
TATCTAAGCATCCATTAGTCAACCTAGCAGACAATAAACTAACATTACCT

FIG. 4 (7 of 61)

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CCAGGTA CTCAAATCAATTCATTGCATCCCAAATCCCAGATGGGCCACC  
CTTATTGACAAATTCAGCCCAATCTTGGTTGAACACATTTAGAATATATT  
TCCATGAACAAATATCCGGTTGACGAGTTTCTTTAACTTTTGGAGTTTAA  
GCCATTTCTTTTACAGTAGCCTTGTTAATTCCCTGTCAATGCTCCATGG  
GGGT CATGAAGAGACCTCTTATTAAGTGTGAAGCAACTTGGCTCAGGTGC  
AGACACTCAAATGCTTCACATGCAGTGGGAAAAGAGAGTGATTGTCTAC

>Contig26

TTTAAAAAGAACTGAGTCTTTATTAGTCGATTCTTCTAATCTATGAACA  
TAGCATCTCTCTCAAAGCATTTAGTCCTTCTTTAATTTCTGTCAATTAATT  
TTTTAAAAATTTTCATCCTAAAGATTCTGTATATGTTTTGTTGAATTTATG  
CTTAAGCATTTCACCTTTCTTGGTAACAATTATAAATGATTTTGTGTTTTT  
TATTCCACTAGTTCAATTTTCACTGTGTAGAAAAGCAATGAATTTTGTGT  
GTTGATCTTTGTTCCAACATCTTGCAACATTATTGAACCTCAATTTATTAGT  
TCTAGGAGGTTTTTTTCAATTTTCTGTAGATACCTTGAGATTTTCTATAT  
AGACAGTCATGTTGTCTGCAACAGGCACAGTTTTATTTCTTCCTTTTCA  
ATCTATATGCTTTTTTTTTTTTTTTTGCCTTATTGCAGTGGGTAGAAGT  
CTAGCACTATGTCAAATAGCATTTGGTGAAAGCAGACATCCTTGTTCTTG  
TCTTAGAGGAACATTTGGTCTTTAATCTTGATTTAAAAAATTCCTTGCAC  
TAAGTTACCGTGTTTTGCGGGAGGGAGAGGTGGGGTGAGGTGGGGATTTC  
CCCTAATGTTTACAAGCTGGGATTTTCTTTTCTGTGTCTAATTATTTT  
CCTCATTGGCTTGAAAAATCTGATAAAACATTTTAGGACTGTGTATAAAA  
TAGAATTAGCCAAGTGCAATGTCTTTATTGAGAAGAAATTTTCATGGACGT  
TGTGCTACTCTCTTGGCTTCTGGCTTCATGGCTTCCAGATCCACAG  
TAAGCTCTGGATAGTAGAAGTTATAGTAAGACTGACTTCTAAATAAATGA  
AGTGACTTTAACCTTACTGATATGGCTTAAAGAAAAGGAGTGGCCTTTAA  
GATCCATGAACCTTCTCAAACAAAAGTGATAACGTTATCTCCATGCATATA  
TAATACTAAATATAATGCAACTGAGAGAAGTAGGCTGTGGTAAGAAAGGA  
GACCCAAGTGCCATCTGAAGGCAGCACTTACCACTCTGCTTCATCCCACC  
GAGGAAACAAAGCATGAGTATTGCCAGATTTTCTTCTGTTTCAAGAAAAG  
CCAGAAATCCAGGTTTTTGGCTGAAATGTCTGATTTTAAATGTTGGGAAC  
TAATTTATATTTTGAATAACATTGTGTGGGACAAGTGAACCTTGATGTG  
GAACTGCTTTCTCCAGTGGCGACCACTTTGGACCGTTGATACTCAGCAA  
GTTTCAAGCAAGTGCGCCTTGTCAATTGTCACTCATCAAGGTGATGTGTGAT  
TGGTCAAGCAATTAATTTTGTCTCAGCATCTCGTGTGTTTTCAAAGAAGT  
GAAGGTTCAATTGC

>Contig27

TTTCAGAGCACAATGCGTATTATAGTATATTGACTTAATTTCTAAGTGT  
AAGTGAAATTAATCATCTGAATTTTTTATTTTTCAGATAGGCTTAACAAATA  
GAACATTCTGTATATAAATGTGTAAATTAGAGTTAATCTTTCCAATCACA  
TAATTCGTTTTATGTGAAAAAGGAATGAAGTGTCCATGCTGGTGGAAAG  
ATAGAGATTATTTTTAGAGGTTTGTGCTGTGTTTTGGGATTCTGTTTTT  
TTTTAAATTTGTAATATGTACTTGTGTGAATGATTTTTTAAATGATTT  
TACCATTTTTGGAAGGGTATTTAATGATAGAAATATCATCGAGCCAACATG  
CACTGACATAGAAAGATGTCAAAGATATATTAAGTGTAAGTGAAGAGG  
GAAAACACTATGTACAGTCTGAGCCAAATCAAAGCATGTATGTTTTTAT  
ATGTGTACAACAAAAGGTTTGGAAAGATATGCGCCGAATTGTTAAATGTG  
GTTTCACTTGAGGGGGTGGGAGGATGGGGCCCCAGAGGGGTTTTTATGGG  
GGCCTTTCACTTGGTATTTTTTTCATTTTGTCTGTTTGAATTTTGT  
TTTCTTTTTTAAATGGAGTTTCACTCTTGTGCGCTAGGCTGCAATGTAGTG  
GCGTGAACCTCAGCTCACTGCAACCTCCGCTCCCAGGTTCAAGTGATTCT  
CCTGCTCAGCTCCCATGCTCCTGTGTAGCTGGGATTACAGGCACCCA  
TCACCATGCTGGCTGAATTTTGTATTTTTCAGTAGAGATGGGGTTTCACC  
ATGTTGGCCAGGCTGGTCTGTAATTCCTGACCTCAAGTGATCCACCCACC  
TTGGCCTCCCAAAGTGCTGGGATTTCAAGGTGTGAGCCACCACGCCAGCC  
CTGTTTAAATTTTTTATAAGTATGTACTACTTTTGTAAATCAGAATTATTA  
GAAAGCATTCTACTGATTTTAAAGCTTAGACATGTTCAAATGCCTGCAAA  
ACTACTTAACACTCAGCTTTAGTTTTTCTAATCCAAAAAGGCCGGGCAGT  
TAATCTTTTGGTGCCAAATGTGAAATTTAAACGGTTTTATGTTTTTCTG  
TGTGTGAATGAAAAATATTTCTGAGTGGTGGTTTTTTGACAGGTAGACC  
ATGCTCTGTCTTGTTCAAAATAAGTATTTCTGATTTTGTAAATGAAAT

ATACAATATGTCACAGATCTTCCAATTAAGTAGTAAGGGTTTATCCTTAA  
TCCTTGCTAATTTAAGCTTGCAATGCTACTTTACTAAAAGATCTTTGTT  
AAGCTAGTATTTTAAACATCTGTCAGCTTATGTAGGTAAAAGTAGAAGCA  
TGTGTGTACACTGTTGTAGTTATAGTGACAGCTTTCCATGTTGAGGTTCT  
CATATCACCTTGTATCTTGAAGTTTCATGTGAGTTTACCATTAGGATG  
ATTAAGATGTATATAGGACAAAAATTAAGTCTTTCCTTTACCTAAGTTT  
GCTTCTTGACTAGTAATAGTAGTAGATATTTCTGTAATAAATGTTCTCT  
CAAGATCCTTAAATCTCTTGAAATTATAAAATTATTGAAAGACAAGA  
ACAGTTTTTATTATTATATGCATTATTATCG

>Contig28

CTTTCTCAAGAAAAGGGAACTGGAGCAATTAACATATGTAATTTTTTTT  
TAAAAAACCTAAACCTAAACATCTACCTATATACAAAAATTAATTAACA  
ATGGATCATGGACTCCAATGTAAAACATGAACTCTAACTTCTAGAAAA  
AAAAGTGGAGAAAACCTTTGGTACCTATGACAAGGCACAGTTTTTAGACT  
TAACACTAGAAGTGTGAACCTATACAAGAAAAATTAATAATTTGAACCTT  
ATGAAAATCAAATTAATTTGCTCTCCAAAAGACCCTGTTAAGAGGATGAAA  
ACTAAATTACAGATTGAGAGAAAATATTTGTAAATCACATATTTGACAAT  
GGACTTGTATCTAAAAATATCTAAAGAACTCTCAAACTCAACATTAAAAA  
AAATATCTAATTAGAAAATGAGTGAACATTTTACGAAAGGGCCTTATAG  
ATTAGCAAATAAAACACTTGAAAAGATACTCAGCATCACTAGCCATTAGA  
AAAATGCATATTAACCAACAATAATGTATCGCTACACACATATAAGAAT  
GGTTTATGAAAAAATAGTGATGACACCAACTGTTAGTGAAGATGTGGAGA  
AACACTCATACATTGCTGGTAGAAATGTAAAATGGCATAGCCACTGTGGA  
AAATTATTTGGCAGTTCTTTTAAAACATAAAATCAATCTACCACACAAC  
CCAGCAATTTCAATTACAGGGCATATATCCAGAGAAATGAAGATTTATGA  
TCACACAAAAATCTGTACACAAATGTTTTATGGTCACTTTATTCTAATA  
GCCAAAACCTGGAACTATCCAAATGTCTTCAATGGGCAAAGGATTAAA  
CACACTGTGATACATCCATACCATGGAATACTACTCAGCAATAATAAGGA  
AAGAATTATGCTACACACAAGTTGGATTAACTCAAGGAAATGTGCTG  
AGTGAAAAATTAACAAGCCAATCTCAAAGGACACATACTTCATGATTCCA  
TTTGTATAACATTAATTAACACAATTAATTACAGAGATGGAGAACAGAAT  
AGTGGTTGCCAGGGATTATACATGGTGGACGCGGTGAGGCGGGCCTCCAC  
GCCTTGGAGATGAAGGGGGCTACACCTTTAAAGCACACCCACGAGAGAG  
TTTTGTGCGGAGGGGCCAATTTAAGTACTCCGCCCCGGGGGGGAACAC  
AGGGGCAACAAAAAAATTTGGCCTTGGGGGTGACCAACACAAAAAA  
AAAACAAACACACAAAAAAACAACNATGGGTGGGAGGATTAATCGCCAAA  
TCTGAGTAAGCTATCTGGACAGTACCAATATCGATTTCCCAGTTTTGATG  
TTGTACTATAATAATGCAAGATGTTAACATTGGAAGAAGCTGGCTGAAGG  
GGGCTCAGGAACTCTCTGGACATTTCTTTGTACCTTCTGTGAATCCATC  
ATTATTACAAAATAGGACATTTTCTAAAGGTTAAATCATTTTAATTTTAA  
AATGTCCCTGTTACTGTTGAACTCACATCTCCATATACTGATCAAGAAC  
AGCACTAATGGCCCCCTGGCCTCCAGGAATTCACAATTCCTACTGACTTTT  
CTTTGAAACCTTGGCCAAGTCGCTTCTTCTCTGCTCCTCAATTTTTCA  
TCTTCAAAATGAAGATTGAATGACTATTAATCTCTTGCAATTCCTGAG  
ATGAAGGGTCTTAAAGGAACTGAAGAGGATGCCATGTAATGTAAATATGG  
GTTTTTACTCCATCAGCCAGCCAAGACAGAGGGCAGACACCAAGACATGG  
TAACCAAGGAGGCCATGTGTAACAAAGACCATTATAGACTTATGCTCTGG  
CCTTTGCAGCCCAACTGGTGTGGCCAGTTGGTGGGGTATGAAGAAAATGG  
GGCCTTCCAGGAACCATGTTGAGTGGAGATAAGCAGGGAGGAATGCAGAA  
GACATGGGGGCAGTGCCAGTCTCAGCCCGAGCCAGCTACACCCACACATG  
GTTATGAAAGACTGACAGCCTGTAAGNTGAACACAGCCCTGCCTCTCTTA  
GATAGGC

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GCAAAATATGATCTCAGATGTGGATTTACTGTAAAGTTCATCAAATTTAAA  
TTTCAGAACACTTAATCTGCAAGAGTCCTTTCCAAGACCTTATACCTAAT  
TTTGTGTTTACAATTTTATATTTGTTTTCTTAAAGAAGACCACCAATATA  
AACTATATCCAGCCTTCATGATAAGTACATAGGAACTATGCAATAAAGG  
GGGAAAAAAAACAAAGAAAAATACCTAGTTTACTAATGGTTCACTTCTGA  
ATAGCACATATTCATAATGATACAAGCACTCATTACTAGTCTAGGAAAAT  
GAAGATATAATTGCATTAGGAAGATCAAGAGGTAGGAAATGTGGATGTGT

FIG. 4 (9 f 61)

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GTGGTATAGACTAGGGCAGGACAAAGAACCCTAAATCCTCATTTTCTAAAG  
ATAATTGTTAATACGTAAACTCAAAATTCAGAAGTAACAGTAAAGCG  
GTCATTAAGAAACAAGCACTAAACACCAGATAGGAAGCGAGAGATGGGGG  
AAGAGGGCGACAATCTGATTATTTTTGCAACAAATTTTGTAACCATT  
TGACTGTTTACATGTAGAAGTTGGATCTTTTTTAAAAACACAAAATAAT  
AATACTATTATTTTTTAACTGGATTTTTGAAAAAGAAGATAAAAGTCTCA  
TTTTAGTAATTAAACTCATTCCAGGTTAGTCCACTCAAACTTATATTC  
GAAAATTAAACTTTGGGAGGCTGAGGCAGGCAGATCACCTGAGGTTGGG  
AGTTCGAGACCAGCCTGACCAACACGGAGAAACCCGCTCTCTACTAAAA  
TACAAAATTAGCTGGGCGTTGTGCATGCCTGTAATCCAGCTACTCGGGA  
GGCTGAGGCAGGAGAATTGCTTGAACCCGGGAGGCAGAGGTTGCAGTGAG  
CCGAGATCACACCATTCAGCTCCAGCCTGGGCAACAAGAGTGAAACTCCA  
TCTCAAAAAAAAAAAAAAAAAAAAAATTAACCTCTGGAAGTTGAGTTTG  
CAAATATTATTATTTTAACTTGTATGTTTGGAAAATGTCATG  
ATGAAAATTGAGGTTGGGGGATGAGAAAAAAGAAAAACATCAACCCAC  
AGCCCATTCATTTTCAGCCCGACCCACAGCTCCGGGGAAGGCGAGCAGG  
TCCATCCTTCACTCTTTCTTACCTCTTTCCCTCCTTCTGGCTCTTCCA  
CCTCTAATTTGGAGCCCAAAAAAGGCACTGGGAAATGGAAAAGTCTTTT  
GTACGTGGTACTTGCCGGGGAAGCTGCCATGAAAACCTGGCCCCACGGTG  
GGGAGGGAATGCCANCTGAGGCCTCGTGCCCATGCTAGGATAGACTCGT  
CCAAACATGTCAGGTGGTCTGACAGGGCAAGCANGAAATCATGTATG  
AGTAGAATCTGATCTGTATGCAAGGGCGGGGAGAACACGCGGAGGAATGG  
GGCGTGAGAAAACAGCACAGTACGTTTCTTTAGCAGCTGTCTCTGCTCAG  
CCATGGGAGGTCACAGAGAAAGAGGCTTGGAGGCGTTATTTTCACTGTGA  
GATGTGAGTGTAATAAAGTGCCCAAGACACAGTGAGTACCAGGGAGATGC  
CCTCTTCTTACCCGAATGCAGAATGGCCACAGGCCTTAAACACACACA  
TGGGTCCTCAGAGGAGAGAGGCCTCCACAGTGGACACCCGCATTCTCCCC  
TGGTCAGCAGCAGCGGGCGAGTGCTGGGCCATCATGAAGCTTCAAGGC  
AATGAGCTCTCAGCAATAACAGGAACAGTGCTGGGGGACTGTAGCTGCA  
AGACCGATTTTTCATGTAAGATGGCCTCTGAGGACTCCGAGATACACCAGG  
CTGAGACTAGCTGGCAGCTCCAAGTTGTTGGTCAGAAGAGAACAGGAACT  
AGGGAAATTGGAATTACTGTTACTACAATTCCTTTACATCCGCACAACCA  
TGAGGTCCAGCGATTTTCTATTATTTTTTTTTTTAAGACAGGGTCTCAGT  
ATGTCGCCCAGCATAGAGTGCAATGATGTGATCATGGTTCAGTACAGTAT  
TCACGTCCCAGGCTCAAGTGACCCCTCCTGCCTCAGCCTCTCAAGTGGCTG  
GGACAGCAGTTGCATGCTACAGGCCAGGCTTTTTTTTTTTTTTTTTTTA  
GTTTCTGTAGACACATAGC  
>Cont:1930  
GGTTAACAATGGCACAGGGAAACAAACAGTTCAGGTGCAGGGGCTCTAA  
ATCTATCATAAGATGTTAGGTATGGGGGCTCTGCCGGACACAAACTCAAG  
GCTTTATGCTGTTATCTCTTGAGCGAAATCCTGGGAACCTCGTACATTGC  
TTGCTTCAGTACCTTATCAGTTAATCGGACTCTTTGATATGTTGGGAGTC  
AGCGTACACAAGTTAACTCCTTGAGGAAGGGGGTGGGTAAGGAGTCCTTG  
ATGTCTGGTAAATGAAGGAGCGAAATCGAGTTCCTCTGGCTTTCTCAGCT  
AAGGGAGAGCTTATTCATGTGGAACAAGGCTAAGTGATTAAGGGAGAAA  
GGGAGAGTCTGAAAACAAGGTTAGGTATTACAATGTCAATAAAATTGGTC  
TCCTTATACAGTCCTATGGTAGATTTCTTTCCATCTTTAATCTCCCTCTA  
GCACCACCAGACTTTTCTCTCTGTACCTTGAGATGTAAATTTTGCTATC  
TGAATTTTCGTCTAAGAGTTGTTTCCTTTAATATGCAAATTTAGGGTTAT  
TTAGCTGACAACTGCCAAAGTAGTGAAACAAGTTATCAAGAACTTGAACG  
TCTAAGGTAGGAAAAAAAAGTCTTTATGAATCTATAAGATGTACTTCT  
ATTGGCATGCCTAATACGTCTATGTATTTACGTGTTGTGTACACAGTTTT  
TCACTACTGAAAATATATAGAGGAGTTCTAATTAATTGACTTAAGACAAT  
AAAAGCGCTTGAATCAATACCTTATCAGGAAAAAGGAAAAGACAAGTCA  
AATGCTTGTTCAAGTTTATATACTTAAGTAAAAATCTTTAATAAATAAGC  
TAGCTTTAACATTATTTGAAATGTCTTAAGAATTGCCAGCAGGTTCTGGG  
TTACAGAAGTACTGTTGGGGTGCAAGTGGGGTGAGGTTGGTGGGGTGGGGG  
TGGTACGGGGGCTTTGTTTTTTCTTGCTGCCCCCTTCTGGGTTGGGGAAG  
TGGCAGGACCTTGGCAGCACCCCGAGCCGGCATGGCGTTAATAATGGAGG  
GATGCCAGACCCTAAGTGGCTAAGGCCCGGCTGCAGAGCCAAGTTGGCATT



TCCAGACTGGGGCTCGGGCCGCAACCCTCTCCAGGACCCTCCCCTTGTAAC  
GAGCAGATTGTGCGGGGAGTTTGGGCCAGCTGTCTGGCGTGGAATTTCC  
CCAAATTCAACAAATCCTCCAAGAAATCAATCCATCCATTATCCATCCA  
TCCATCCATCCATCCATCCATCCATCCATCCGTTGGCAGATTATGAAGCAT  
GGATCATTACTTTTGGGATGTGGATATATTAGTTAACAAGGAGCAGCTT  
TCAAGAGCTGGATTTTATGCTTTGGGTGAAGTTTAGAAACTAGCTCCC  
AC

>Contig31

ACCTCATGTGCTCTAGCGCCTCTTACCTCATGCCCTCCACTCTCAGTCTT  
GCACCTCACCTGCCACACTCAAGGGCTTCCCAGGTTCTTCTTAGATTTC  
CACCGATAGCTCAGGGACTTTGCACATGCTACGGTCTCTGCCTGGCTCCT  
CCCCAGATCTTCTCATGCCTAGCTGCTTCTCATCAGCACCCCTCAGAGAC  
TGTCCTGCCCCACCTCTCCAGGTTCCATACCTGCCACCCTCCCCAATC  
ACGTAACAGTTTCTTACAGAGCGAGTTACCATCCCAGTATTTCCCTAAC  
TTATTTTTTGTGACTGGTCTGTGCTGCTCCACCACAAGAACATAAGC  
TGCATGTGAACAGGAGCCTTGTCTATCTTGTACCCCCAGTGCTGTGACA  
TAACCTGATACACATTAGATGCTCAATGATGTTTGATGAATGAAGTGCTG  
GTAGTCCAACCTGTCTTCTTCTTGTCTGTGTAAGTATGTCTGTTGTGGTTTC  
CTAAGAACCTACAGCTCTCCCACTGTGACTCCTGTTCTATGGTCTGATT  
TGCTGGACTAGAATCCTAACCTACATGCTTACTCTTAGTGTCTCTCCCCA  
GAGGCTGAATCCCAGTCCCTAAACCTCCACCAAATGGCTAAGACCTAGCT  
TCCAACCAGACAGGCTACGCTGAGACCTCAGCACCGCCCTTCTGCGGTC  
TCATCCTTAACGCATCCTTCAGGGCCAGCTTAAATGTCTCTTCTCCAAG  
GAAGGCTATCCTCTTCTGCCCCCTCAGTGCTCTCCATGCCTCCTCTATGC  
CTCCATGCCTGCTTTCACACCCTGCAGAGGTGGAGAAGTTGCTAATCTGC  
TGTGTTGACATGTGCTGGGGTGCTTGGGCCAGGGAGCAGGCTGGTGGT  
TGCTGATAGCCCGTGGCTGTGCCAGGTCCATGCTCACTTCTGAGCCCC  
AGTGGAGTAGGCTCCCTTTCCCTTATTGCAGCACTCAGAGGAAGGACGTG  
CTTCTTAGGACAGATCTGGCCAACCTCTCCCTCGTGAGAGAAGGCCAGC  
CATCCTCTTGCCCTCTTCTTCTCTCTGCCCCGAGTAATAAAGGTGCCT  
GGTCAGAGCCTTCTAGAAGGAGACCCAAACATCCACCACACATTCCCAGT  
TCCAACCGTCTCCACATGGCTGGCTGTGCAGGTAAACGCAGAGTCTGTT  
TCACACACCCAACCATCTAGTATTGGATGGGAGGACAGTAGCGTGACACT  
CTTCTCCAGCCTTGAGCCCTACTGTGGGCCCCACCCAACCCAGATACCAG  
AGGAGCCCTGTACTGGGATGCTATTGGATGCTTGTCCAGTCATGTACAAA  
GTTAGCCCTTGTATATAGAGTTAGCTACGTACATCTTCTCTGTAGGG  
AACCCAAGAGGGGAGAAGAGATATGTAGTAGGATTTAACCTGCAAATCCT  
CTGCTGAGCACCCTGCACTACATACAGTGGGTAGCATGTGGTAGGTGCTC  
AATAACTATTGACCGATCTATTGAATACACGTAAGATCGTGACACTATCT  
AAAACGNGGGGTGTGGGGGAAAAACCCCCCTTGTTTAGGAAACCCAAA  
TTGGACCGTGTGGC

>Contig32

GCGCGATTGTGCTAAAGATCATGCATGCCTGATCAAACGTCCCCATATGG  
CGTCTCAGAGTCAACTCCTTCCCACATCAGTGCCCTGACTTCGGCATAACA  
AACCTGGCAGGTTAAGTGATTAATCGGTCTGTACAACTGTAGCCCTTAG  
CAGGAAGCACTAAGCTTCGTTTTTCAATTAATTTCTTCCCTGGAAGTCAAG  
AATGAGGGATGCCTTCCGCCATGAAGTTTGTGCTGATTGTCCACTTTGTT  
CTCAAGGAGATATTCACAGTTTTTAATTTGTCTTTCTCTCCTGCATGGTC  
TCCAACCTGTCCAAGAAGCCAGCTGGCTCCATCATCTGTAAAATCACC  
ATTGTCACCAGAGCACTTGACTTCTGTTGCCCTACAATCCACCTGCACT  
TTATTTCTGCCACCATGATAATGTAGTGTACTACATTTTACATTACAGC  
TGTAAGAAATGTTACATTCATTTACTTAAATCAAATTAAGTCTGCTCACT  
CAGTCCCCACAGTGACCAACTTATAAAGAGAAGGTACATTTAGTCAT  
CACTGGTTTCTCTTACCACTGGAAAACTGAGGAAGGGTCTGGAGTCCA  
CAGTGGTTAACATCATTGCCTCTGTTTTTTCTCTACTCAATGTAACCAT  
CCAAGGTTACTCACAAATTCACAAAAAGAGGTCTTACCTCTGCTCTCAA  
GACCCAGAGGGCTGGGTTCTAACTCAAAGGCCAATGTTCCCCAAGTTTT  
TGCAATTGTTTCAACATTGGGGAAAACTCGAGGGGATTCAAGAATGGTTAT  
ATAAGTTTTGTGGAAAAATGTATAATTTTTTAAATTAATAACAAAGTA  
TTATGGAAAGCACTAAATATTGAATTTATATAAATATTCCAATATTTTT

CTAAATTTTGTAGTGAGAACTTGAGCTTGCTTCTGTGAGATATTTATTTT  
AAAACAGATTTGACACTTAAATGTCTAATCAAGCCTTTTAAACCATGAT  
CTATCTCTTCAAATTTCTCAGATGCCACCATCAATAAGAACTTTGTTT  
ACACAAGTAAGTGGTAGCAATGGCAGGGTGTATCATTTTTTTTTTTT  
CTTTTTTTGAGACGGAGTCTCGCTCTGTGCGCCAGGCTGGAGTGCAGTGG  
CGCGATCTCAGCTCACTGCAAGTTCACCTGCTGGGTTCACGCCCTTCTC  
CTCCCTCAGCCTCCCGAGTAGCTGGGACTACAGGCACCTGCCACCACGCC  
CGGCTAATTTTTTGTATTTTGTAGTAGAGACGGGGTTTACCGTGTAGCC  
AGGATGGTCTCGATCTCCTGACCTCGTGATCCGCCCGCCTCGGCCTCCCA  
AAGTGTGGGATGACAGGCGTGAGCCACCGCGCCCCCGCGTGTATCA  
TTTTTGCCTGATGAAATTTTCCTTGCCACTACTCTGGATGGTTTGATAC  
ATTTAAATGTGCTTCCAGGGTACAATTATCCTTTAAATCTATACCTCTT  
TCCTTTCTTTTATTGACAAATATAATGTTACACTTTTCTGTCAATTGCAGC  
CACACCACAGTACACAGATCCCAACAGAGTTGTAATATTTTATTAGTTT  
CAGAGTTTCAATATTTTATCACTTTCAATACTTCATGTGCAGGAGTTTAA  
TTTGGTACTTCTTTACAAATAAATGATGTGCTTCCAAGCATTTCTTTTC  
AATAATTCCAATCAATGTTATTAACTGAGTAATACTAGTATCTGTTTATT  
CATAAATTCACAGGAAATGCTTTTTTACTTATTAGTCTTTGGAATCTGT  
TGTTTGTATAAACATCTTTCATGATGGCTTTGTGTCTACCAATAGCACTA  
TTGCCAAAAGGCACCTTTTTCTTGTTCTTTACTTCACTGGTCCGAAGCC  
TGGTACCAACAACCTACCACACAGACTGGGAAATGAGCAATTTTGCCACGT  
GCCCTTAGCTATTAATGGTGGCACTCCATAACTAGCATCTTAAGCTCAAT  
TTCATGAAAGAAATGTGTTTCTTATTTTGTACTTGCAGGCACCTTTTAAA  
CTTGTAATCTTTTATTCACTTTTAAATTAACACAGAGTAATAGAACC  
ATAGAAGGAAATCAATACCCACGAGTCCATACTGATATAAATAAATAGTT  
ACATAAATAAATGGGGGAGAAATAACAGCTCTTCTTACAGAAAATTT  
CAATTAATAAATGAAGAAGGAATTAGGGAAATACAACGTTACCATTAAGC  
AACCACAGTAATAATCATTACAGGCAATATCCAAAAATAAATTCCAAAGC  
CAGTGGGCAAAAGTTTGAGGAGATACAGGATATTAACATAGTCTCCAAT  
AGCTCATGCTATTTATAAATTACAAAAGGAAACATAACAACGTGTATAGTG  
AAGAAATCAGCAGACACCACCTTAGCCAAGTGATCAAGGTTAACGTCAC  
TAGTAATAGGGCTTGTTGACATACTGGACTCCAATCTGATACACTGATAA  
GGACACATGACTTCTGCAGTATTCTTACCAAAAACAGAAATCTAATGTAA  
TTAAGGAAAATGTCAGACAAACCTATTCTGAGAAACATTCTATAAAACAA  
CTAACCAATACCTTCAAATTTGTCAAGGTCATAAAGACCAGGCGATGGTC  
ACAGATTTGAGGAGACTAAGGAGATACAACAACCTAAATACACAAATGGAA  
CCATGGCATTCTTGATTGGATCTTGAAACAGAAAAGGATATTAGGAAGA  
AAAGCTGATGAAATTCTAATACATTCTGTAGTTTAAATTAATAGTATTGTA  
CCAATATTAATTTCTAGATTTGATCATTATACTATGGTTAAGTTTTTAA  
CATTAGAGGAATCTGGGAGAATGGTATATATGAACCTCACTGTTCAATTCA  
ACTTTTTCAGTAACTATTATTTCAAATAAAGTT

>Contig33  
GGGAGCGGCGGCCACGCTGATCTCTAAAGCTTTAGACCACATTGGCTCG  
AGCATGGTCATGGCCGTTTCCTG

>Contig34  
GACGCTTAGCGCTATATTATAAAGAAATATTCACCTCCCTGCTGAGCTT  
ACAGGGTGACCTAATGTCCAACAATATGAAATCTCTTCAATGAATTGCA  
GCACGTCCATATATAACCCACATGGAAGCTGTCTCTTCTCCTCACCTTCG  
AACTTCCCATGCCAAAGAGGGACCTCTTGACTCAAATACATCTTAGCAA  
TATAGAAGATGCTGGAGACTTGTAGGAGAAGTGGAGAGGGTTTACAGTGT  
AGCCCCACAGAAAACAACTTATGACCCCATCAGTCACTTGTCCCTTTTT  
CCATGCCTCAGTCTAGTCAGGAAACCACTAGATCCTGGATGGCTTCTTCT  
CCCTTCCCCTCCTTCTCTTCTCCTCTCCCTCCCTTGCTCCTCCTCCTC  
CATCACCCACTCCTTACTTCCAACCAAACTTGACTAGCTCCAGTCTCAT  
CCCTCCTTATTGAAAATTTTTACTCAGCCCTCCTCCCCCACTCCTGCC  
CAATCTTTATTCTTACCTACATCAGACTTCACCAAAACAAAGGCCAGGA  
TAATAAACAGGACAACTCTTTCAAACACATTTAATGACCATATTTGT  
TATTTTGGTACAATTTGAGGAGTCCCAATCCCCAGGGAAGACTAACAGA  
AGTTCTCCTAACAAAGGTGGGTCTCCCTTACTAAAACTCCTGTAATGG  
CTGAAAAGAGCATGAGGTTTTCTGCATATCATTACACATTCAATAGAACG

FIG. 4 (12 of 61)

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TCATGCAGCTGTTAAAAAGATCTGTAGAGGCTATCTTGTGACAGAAAG  
GCATTGGAGATATACTGTTAGTGACAAAAATAGGTTATAAATGAATTTTT  
CCATGCATGCCTCTATATTTATAAATACACACACATAAAAGACAGGAAGG  
ACAGACATTAAACATTATAGTGCTTAAGATGATGCATAGTATAATAGTT  
AGGACCATGGCCTTTGGGACAGAAAACTACAGCCTCTCTCCCACTTATCA  
GCCATGGGACCTTGGGCAATTTGCTCAGCCTCAAAGCCCCTGTTCCCTTA  
TCTGTGTGCTGGGGTTGTTGTAAGAGTTAAGTGCAATACACAGAGAGAGA  
GAGAGTACCTAACATGTATTATGTGCTCAGTCAATATGCATCATAGTACT  
CATTGTTACATATGTTCCCTAAGTGCTTTATACGTTTTTTCCCTAAGTTGA  
CCATCTGTTTTTGGCATTATGAAACATAATGATCCTAACAAATTAATAATT  
AAAAACATAAAGAATATTTGCCCCAAAAAATAAAGAACATGAATTCCTTC  
AAGTAGCCAAGGGGCCATAGACAGAAGTAAGCCCTTGGTGGGGCTTAGTT  
GAGAGAAGTCTCCAGAAGGTCTTTCGTGTGTTAAAGAAGAGGGTAACAGG  
GAGGAGGTGGGGAGAGATGTTAACTGAGTCTAAATGAGCACCTGGAAGAA  
GAGATGGGACAGGCCACTTCTGCCTGGACTCCCTGATTGTTAAGAAGAAT  
GAAAAAGAGCAGAAGTCTTCCCTGAGCCCACTTCACTCCCTGACTTAAC  
CTAGTCTTTTGGCCCTTCCCTCTCACTCATGGCTACTTTCTGTGGTCACCT  
TGTTGTAGAAATGGATGTGACAGCCACCTCATTTTTTCTACCTCCTTCAC  
ATGTTTTAGATAATTTAATGTAGTAGAAGACGGTTACAGCAAAAAATTAC  
AAAAATCAAAATATCTCTGCTATCTACTGTTGCATTTCTAACCATCCCAA  
AACAGTAGCTGAAACAGCACTCGTGGTGCAGCGCGGTGACTCATGCCTT  
TAATTCAGATACTCCGGAGGCTGAGGCAAGAGAATCACTTGAACCCGGA  
AGGTGGAGGTTGCAGTGACTCAAGATCATGCCACTGCACTCCAGCCTGGG  
TGACACAGTGAGACTCCGTCTCAAAAAAAAAAAAAAAAAAGCACTCGTG  
TATTTGTTCAGATCTGTGGTTTGGGCAGGGCAGGGCTCAATGAGGACA  
TCTCGTCTCCGTTCCCGCAGTGTGAGGAAGTGAAGTGAAGTGGAGGGT  
CACACAGAAGATGGCTCCCTCAAGTGGCCAGCAAATGGTGCTTACAATT  
GACAGGGAGCTGTTGACCAAGGGCCCCAATTCCCTCTTCTATGGCCCTT  
CTCGGGCTGCATGGGCTTCTTTACAGAATGGCAGCTGGATTCCAAGAGCA  
AGTATCACAACTACAGAAGAGTGGAGGAATATTGAAAGTTCACAGTCTC  
TTAAGACGTTGGCCAGAACTGGCAAAAGCTTCATTTCTGCCATGTTCT  
ATTGATCAGTCACAGAACCTGCACCAATTCAAGAGGAGAACATATAGAGG  
ACATCTCTCAATGGGATAAGTGTCAACAAATTTGCATCTATCACAATCTG  
TCTTTTGGGTACAACTATTTCTATTCCTCCATTATGCAAAATATACTCA  
CAACCTCCAGGGGTGCAAAAGCCTCATCCATTTATGGCAAATGTGGCC  
CTTTTAATTTATATAAAATAATTTGCGGGGGCTTCTTTATATTTTAAAC  
TCCCCTGC  
>Contig35  
GTGCAGAGAAGTGATTTAAAGCCCTTCAGAAAGAATGCTTTATTCCCGTG  
GAATTTGGTAACTTGCTTGGGTGTGGGGAGGTTTGTGACGCTTTCTCCACT  
CAAATTATCAGACCCTTTCCATTTAGTGGTAGACCATTTCCTCGTCCAG  
GCCAAGGGCACATAGTACAGAGAAATAGGGAGTTGTTACCCAGGGAGAGA  
ACTTGGCTCTAAACCTGTAATAGAAAGGTGAGTTCTGGTCTGGAGGGTCA  
ATTTTGATCTTTGGCTCAGATCCAGGAATTGGAACCAAGGCTTTTGAACA  
TTTTAATGCAGGGGATTAAAAAATGATACGAGTCATTACGAATATATT  
TGCTTAACATCTAAAGAGATCCCTCAAAACACTAGAAAAAATAAGAACAA  
AAATCTAATAAAACAAAATTTGTTAAACACATTTACCAAATTTTTTTTTT  
TGGTAAAAATTCAAATGTCATAAATAAAGCTAAAGTTCCTCTTGATGACT  
CGCTCCTCTGCCCTATTCCTCACTCCAAGTAACCACTATTATCAGTCTTGCC  
AATACCTTCCAGACCTCTCTACCTCTATATACCATTAGAAGCACATGGT  
TTTGCAATGAGGATGTGCAAGTGTGTTTTGTTTTACGTAAATGTTATCACTCT  
GTTCTTGTTCATAATTTGCCTTTTTCTCTCAATGATTGCTTGGCTATC  
TTTCTATTTAGTAGCATCTCCTTTCTTTTAACTTACCATGTTTATTT  
AACCTTGCCTCTATCAACAGATATGTAGGTTGTTTCTAGTTGATTTCAAT  
AAGTATTTATAAACAACGCATCAGTAGATGTCCATAAATTTCTTTACGGA  
AGATGGCAAGTAGTGGAATTGCTGAGCCAAAGAACATGTTTAAAAAACCC  
AAAAAACTAGACGCTACCAATTTTCTCTCCAAATGGCCATACCCACTT  
ACCCATACAGAGATGATTTGGAATCTGGCTTCCCTCACAAGGTGAGATGCC  
TTCACAGTTTCATTCTTCTGGCATGTCTCCCTTTTGTATCTGAGAGAG  
CTGGCAGAATTGTGTCACTAAATCAAGGATAGAGGGTCAAATGACAGCTC

FIG. 4 (13 of 61)

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AAGCTCACAGGCACCTCTGCTTTCTTCLAGACCACCTGCTTTCCTGCCA  
CCAGCTCTGTTCCATCTTATAGAATGGTTGCCACTTGGGTGTCTGCTCCG  
ACAGCCATGTCATCCTTTGCACTGCAGTTATGAAGCAGACAGAGCTAGGA  
GAGGGGCTTTGCCAGCCTCTGCCCTAGCTTGGAGAACTTCAAAAAAGGAG  
GGTATTGAAGTTGAACTCCCCAAAAAGGGGTGGTCCCCACACCTCAAAA  
AGTGGTGCCTCCGAAAGAAATGTAAAATTCGTGTGGGGGGGAAAAAGGT  
TATTTAGAAATTGTTGGCTTGTCTGCGCGAAAGTATGTGTGGTTACGGGG  
AGTACGGAAATTTGAGGGGTGGGGGCGAGGCCGTGTGTCTTTAGCCCG  
GGGTTTTTCCCGTCGCATGTTTAAGGGGGGGAAGAGGGGGATGTTTTCT  
TTCCGCGAAGGTTTTTGAAGAACGGCGTGG

>Contig36

CCCCCACC GCCACTACTCAACCGGCCGTTACGAAACAACCTGCCACAT  
CCACTAACCCGCTGGCTCACCACCCACCGCCCTCCCGATCCCCCAATCC  
AAACTCAACCCCCACCACCAAGCGCCTCCCCCTCCCCACCCCTCCAGCT  
CAGCCCCAACCTACCACCAACCCCGACTCGCCACCGAAAACCAACAGCA  
AACCCAAATGCCACAAAACCAAGTGTCCAAACCCCTCCTTCCCATCAGTTT  
GGTGGGCCCCATCACCGCTTCCCCTGGCCCCAGGCTCTCCTTTTGTGCGCTT  
GGAGCAGCAGACTGATCTCCAGCCTTCACTCACTTCATGTGGTAATCTG  
TTGTGTTCTCACTGTGAGAATCTTCTGCATCCCCTCACTACTCTGCTGA  
AAACACTCTAGTGGTTCTCATTTGCTCATTAAATGAAAGTCTAGATATTAA  
ACGTAGAAGGCCCAGCACAATTTGCCCTTATGCCACCTACCTCTCTAATC  
TTTTCTCCTTACTCTGACAGACTCTCCGTCTGTCAATTTATGTATTCTTTT  
ATTGCTCTCTTCTACTTTTAGTATGAACTGGATTTATGGATTTTTTTAAC  
ATTGCTTTCAAGTATGGAATAAAGAATTTTATTTATTTATTTATTTATTT  
ATTTGAGACTGGGTCTCACTCTGTTGCCAGGCCAGAATGCAATGGTGCA  
GTCATATCTCACTGTAACCTCGAATTCCTAGGCTCAAGCCATCCTCCTGC  
CTCAGCCTCCTAAGTAGCTATGACTACGGGTGTGCATCACCACATCTGGC  
TAATGGAATAAAATATTACAATGCCTAATCTTAATTTTCAAAATTTTAAA  
TTACATTGTACCTAATGCCCATGCATTTACTTTTTTTCAGTGGGTCAATAG  
CCCTCACTTTGGCAAAGGTCCCAGGCCCAAGGTAAGGCCTTACTTTTTCC  
AAACTCATCTTTTGAAAGACATAAGTGCCTGTAAGTTGTACCACATTAGG  
TTCTAGGAATTTTTCATCAAAGACTTTATCAGACTATTTTCTCTAAGTT  
GAGAAAGAGCTGGGGGCGAATATGGCACTGAATGACTGAAGAGAAGGCA  
CTGAAATCAGGCCAGAGGTTGCTGGAAAGAGCAATGAGGAACACCAGCAG  
CAATGAGGAGCCGGTGATGATTTTGGCTTCAAGGGAGGTGTGTACCACA  
CCGATTTTATCTCTACGTGGATGAACCACAGCTGTCCGGCTCCCTTGTCTC  
CAGGACATCACACTCTCCACATTCCCTCCCATCTTCCGGCTTCTGCTTCC  
CGGGGCCCTCATCTGCCCATCCTGGGTGAACACTGGTCCGTCAACTGCT  
GGGCGTACCTTCCCGCTCTGCACACCCTCCCTGGCCACCCCACTCTCT  
CACGGCTCGCACTGAGAGGAGCCGCATCTCTAGCTCCAGCCCATCTGCC  
TCTTCTGAGCTCTAATCTCATGTAGGCGACTCCTGCCGGTGTTCCTCAC  
AGGCCCATCATACTTCAAAGCATTTTCCCCTCAGAACACCATGTCCTGGC  
TGCTCCCTCCAGAAGATACATCTCTCAAGCACATCCCCGCGGCTCTCACC  
TGGATGACTGCATTACCTTCTCCACATTTGCCCCCTCCTTGGATGTA  
TATAGATTGTTTTAAATACAAATCTGATGTGCTTGTCTCCTGCTTGAA  
ACACCTCAAACTGCCTTCAAGATAAACCACTGCCCTTGACATGTTTACA  
GGTTGCCCATGGCCTGGCCCTGCCCATCTCTTACGCTCATCTCATGCC  
CTTGCCCCCTCGCTCTCTGGGCTTCTGCCTCCCTAGCCCTCCTTTAGGTTT  
TCTAACACACCATAGTCTTCTAGTGTGGGGCCTCTGCAAGTGTCTGTTT  
CCATTGCCCTGAGACATGAATCCCTCTCCCTATCTCTACCTGCACCTTCAT  
CTGATTAATCCCTACCCTTCTACTCATGATGTTGCTTTCTCAGGGACTC  
TCTCTGACTTTTTAACTAATCAGGGTCTCCCCAGTATATATCTTCATAG  
CACTCTGTATTACTCCTTTCTTAATGACCACCTGCTGTAGACAGAATGTT  
TGTCTTCTCCAAAATCATATGTAAAACCTTCCACCAGAGCGATGATTAG  
AGAAGCCTCCC

>Contig37

GACTGACATTGAGAAGATATTAATAAGAGCACTAATGATGGGGATTGCAA  
CCATGTCTTTACTGACTTCCAGAAGCTTCTTACAGTAAACATGAAATCAC  
ATAATTTCTTCCACTTCTCTACTGTTTCTTGTCTGGGCTCTGTCTGCT  
TACTGTCTAATATCTTGGCCCCCTTAAAAGTTGCTAATCTTCAAACCTCA

TTCCTGTGACTGGGCGCTGGTCCTTG...CATGGGCCTTGAAGATAC10A  
CTGTACACTTATCTGGAGCATCCAGTGCCTACCACCTGACCCAGATTCTT  
CATTGCGCTCCTCCCTCCTCCACCTAATGGGATTGCTCATACCCGTGTG  
GGACCCCTCCCATTTCCTCCCACTGAATACTTATCAAGACAACGCATTGC  
CATACTCCCTCGTACCCTGCTCTGGGCATCAGACTGAATGTTTGTTCCTCA  
TTGAGGATCTGCAGCTGCATCAGTTTCCCCAGCACCGTCCAACCCCTTGA  
GCATGGCTAGTCCTAAAGCAGAGAATTAGCCTTTCTATCCCTGCTGCTAT  
ACATGCTGGGACAAATAATAAGAAATGACAGCATTATGATAATGCAGG  
CTGCAGGAGGCAGGAGGCAGGAATCAAATTCGTGCTTATCAAATAGTGCT  
CCAATTCCTTTGAATATTGGACTATAGAATATGTCATGGATCTATGCTCAG  
GTGGGTTCCCTATTACTCACTCCACTGAGGCCAGGTTGTGGGATTAGCTG  
TCCAAGAGGGAGTTTCAGTCTCACAGCATAGGGTCATTCTGAGAATTACT  
GGCCACACTTGTGTGGAGACCTCCAGAGAACAGAATCTGGGTTGTTGCC  
ATGTACTTCAGGAGGAGAGAAGTGGCAGGATGCCAGCCCCACAATCAG  
AGGGGAAGGGGCAGAGCCACATGTATGAAGATCCTCTCCCCAGTACGTGC  
CAATCAGAGGGCTTCCTAGCTTTTGGGCCAAGGAAACAATGTGGGAAGCA  
AAAAGGACAACTTTCTCCTCCCTTTGTCATGAAGACTGAGCAGTTTACC  
AGATTCCCAGGGAACACCCCTTCCACTCTGGGTTGAATGTGAGTGAGAGA  
CATTGAGCTGGAACACTAGAAAACTATTTCTGAGCCACTCACCTTTAG  
CCCTAGAAAGTGTGGATTGTCTCTTCATCTTTGCCACAGTAGAGACTGC  
TGATAGCATCAGAACTTGGGCTCTGGAATTAGACAGATATGGGTACAAAT  
CTGAGCTCTCTCACTTATTAGTGTGGGATGTAGAGCAACTTTTAAATCC  
TTCCAAACCTCAGACTTCTCATGCATGATGTGAGGATTGTAATAGGGCCC  
ACCTAATAGGGGTTTTTGGAGAATTAAAAAAGTTATTCAATGAACAGCATT  
TAGCAAGATGCCTGACCATTGAGAAAAATAACAAATTGTTTATTATTATG  
TTATTATTAAACATCTTTCTGCACCTTCTGACTGGGGGCATCGTATCAT  
CAGAAATACTTAGGATGGGATGGATTCTGTCATGGGCTGAGTCAAGGGTG  
CAATAATGGAGGAGTGAAGAAGGAAGAAATGGAGGCAGAAATCCCCAGGA  
GCCAGCATGGTACAAGGCTGAGCTAGTGTGTCAGAGCCTCCTTGGAAACA  
GCCACAGAGCTTGCATCTGGCCCTGGAGGAACCTCTTCTAGCTGGCAGGA  
CCAGCCACAACAGTGGCCAGGGGATTTCAGGGCGTGGGCTCCTCAGGA  
GTTCAATTTGGACCAAGCCTGCCTGGAGAGGGGTTATAACAGGGATCCTTC  
CCTACTGGCAGGTGATTTACCCCTCGGTGAGAAGCTCAGGCATTTGTTTG  
ATGGAAGGTGGAAGGCCCTGTGCTGGGCCAGTGAATATCAGGGATGGGCG  
GGTGGCTGGAAAATAGCAAATAAGACAATATGATAACACAGTTAACCACC  
ACACTATGTGAAGCTACAATATGGGTATCTGTAATAGACAATTCATGT  
AGAGAATAATTTAAGGTGTCAATCTCCCCGCCAATGCCATAAGCACAGG  
GCCTCTGCCTGGGTTTCTCACTGTGGAATGTCTCTCTGGTCTCTCATGC  
CCAGAGAGTGGGAAGTACTCTCTACTTTAACACCGGCTTTCTGTCAATTC  
CNTGCAGCCCTCCTCAGCCCCCTCTGCACAGGGAGGTTTCTCCTGCTG  
CTGCAGTGCTTTGTACTTGTAGTGGTACCTGCACACAGGTATTGGTGTG  
CTTGTCTCACCACCTACATCACTGTAAGCTCCCCAGGAGCAGGCTTCTT  
GTTTGACTCACCTGTGATCCTCCACCTCCCACCCTGTAGTGCCTCAAGCA  
TTCTGTAGAGCATGGACGCC

>Contig38

GACTAATAAGTACTTCATTATTTGGGTATTTTCCAAGAACACATATTGT  
AGGAAACCATTCTTTCTAAAAAAAAGTGTCTTTTAAAAAGGTGAATA  
ATTTTGTCTAATTCAGGTTTATTGAAAAGTTATGTATAAAACAAGGTA  
AAAGGAACAAGGAAATAAGGGAAATGTAAAGAAAATATAGAAAATAAGT  
GGTATTTTGGTAAGAAAGCTTAAAGAGAAATAATTTTAGGTAAGAAAG  
AATCTTACCTAAATTTTGTGCTAGAATAAAGTGACTGGCTAAGAAAGG  
ATGTTCAAAGCTATTTATGACAAACCCACAGCCAATATCATACTGAATGG  
GCAAAAGCTGGAAACATTCCCTTTGAGAACTGGCACAAGACAAGGATGTC  
CTCTCTCACCCTCTATTCAACATAGTATCGGAAGTTCTGGCCAGGGCA  
ATCAAGCAAGAGAAAGAAATAAAGGGTATTCAAATAGGAAGAGAGGAAGT  
CAAATTTTCTCCGTTTGCAGATGCATGATTGCATATTTAGAAAACCCCAT  
CATTTCAGCCCCAAAACCTTAAAGCTGATAAGCAACTTCAGCAAAGTCT  
CAGGATACAAAATCAATGTGCAAAAATCACAGGCATTCTATACACCAAT  
AATAGACTAACAGAGAGCCAAATCATGAGTGAATCCCATTCACAATTGC  
TACAAAGAGAATAAAAATACCTGGGAATACAACCTTACAATGGACATGAAAG

FIG. 4 (15 of 61)

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ACCTTTTCAGGGTGAAC...GCAAACCAC...CTCAAGGAAATAAGAGAG...A  
ACAAACAAATGGAAAAACATTCCATGCTTATGGATAGGAAGAATCAATAT  
CGTGAATATGGCCATACTGCCCAAGTAATTTATAGATTCAATGCTATCCC  
CATCAAGCTACCATTGACTTTCTTCACAGAATTAGAAAAAACTAATAGCC  
AAGACAATCCTAAGCAAAAAGAACAAAGCTGGAGGCATTG...GCTACCTGA  
CTTCAAACATACTACAAGGCTGCAGTAACCAAAACAGCATGGTACTGGT  
ACCAAAACAGATATATAGACCAAAAGAACAGAACAGAGGCCTCAGATATA  
ACACCACACATCTACAACCATCTGATCTTTGACAAACCTAACAAAAATAA  
GCAATGGGGAAAAATAATCCCTATTTAATAAATGATGTTGGGAAAACTGG  
TTAGCCATATGCTGAAAACGAACTGGACCCCTTCCTTACAACCTTATAC  
AAAAATCAACTCAAGATTGGAATTAAGATTAAACATGGCTGGGCATGGTG  
GCTCACGCCCTGTAATCCCAGCACTTTGGGAGGCCGAGATGGGTGGATCAT  
GAGGTCAGGAGATGGAGACCATCCTGACTAACACAGTGAAACCCCTGTCTC  
TACTAAAAAATACAAAAAATTAGCTGGGCATGGTGGTGGGCGCCTGTAAT  
CCCAGCTACTTGGGAAGCTAAGGCAGGAGAATGGTGTGAACCCAGGAAGT  
GGAGGTTGCAGTGAGCCAAGATCACGCCACTGCACTCTAGCCTGGGCAAC  
AGAGTGAGACTCCATCTCAATAAATAAATAAATATGGAACCTCTCCCAACA  
CAATAATAAGACAAACCCCAATGTTTTAAATGGGCAAAAAATATTTGAA  
CAGACACTTCAAAAAGAGGATATGTAAATGGTCAAAAAGCACATGAAAA  
GATGTTCAACACCATTGGTCATCAGGGCAAAGAAAAGTAGAACCAATG  
AGATGCCTCTGTACACCACTTAAATGTCCAAATTAAAGAAAACAAGTTTT  
GGCAAAGTTGTGGAGCAACTGAAATGCTCGTGTATTGCTGGTAGAAAAAC  
AAAATGGCATAACCATCGCAGATAATTTGTTGTGAGTTTCTTACAAAGTT  
AAACATATACTTATTGATATGACAGTTCATTCCAAGAGAAATGAAAAACA  
TAAGTCCACACAAAGACTGTACCTGGGTGTTTATGGTAGCTCTATTTCAT  
AATTGCCAAAATCTGGAAACAAATCAATGTCCATCAGCAATGGAATGGA  
TATACAAATTGTGGTACACATGTACAATAGAAAAGTACTCTGCAATGGAG  
AGAAATTAACCATTTGACAAACACAAAAACATGGACAAACCTCAAAAAACAT  
TATGCTGAGCAAAAGAAGCCAGACACAAAAGACTGCTCAGCGCATGATTC  
CATTTCATATGAAATCACAGAAAGGGTCAGTTGAAGGTGCAGAGACAAAAA  
GTAGATCTGCAGTTGCCTGGGGATGGGGTGGGAGGTTGACTGCTCTGACG  
CGTAAGGAATTTGGGGGTAGGTGGGGGATGGTGGGAATATTTTGAAT  
TGAATTGGGTAAATCTGTAATAGGTAAATATTGGACCCACAGTATTT  
GAGATAGGTTTCAGTCAATTTAGACAGTTTATTTTGGCAAGGTTAAGGAT  
GCATCCGTGACCCAGCCTCAGGAGGTCTGACAACCTGTGCTGAAGGCAG  
TCAACATACAGCTTGCTTTTATTTCATCTTAGGGAGACATAATACATCAAT  
CAATGCATGTAAGGTTTACATTGGTTCAATCTGGAAAGGTGAGGGAACTT  
GAAGCAGGGAGCTTCCAGGTTACAAGGTAGATTATTCTCAACAGAAAGGA  
ATGTCCTGGTTATGATAAGCGGTTGTGGAGACCAAGGTTTATCTTGTAG  
ATGAAGCCTCCGGGTAGCAAGCTTCAGAGGGAATAGATTGTCAAAGTTTC  
CTATCAGACATAAGGTCTGTGTTGATGTTAATGCTGGTCAGCTTTTCTCTG  
AATTCCAAAAGGGAGAAGGGTATACTGGGGCATGTCCAACCTTCCCTTCC  
ATCATGACCTGAACTAGTTTTTTTTCAGGTTAACTTTGGAATGCTCTTGGCC  
AAGAAGAGGGGTCCATTAGATGGTTGGGGGGGCTTAGAATTTTATTTTT  
GGTTTACAGTGAAGACTTTTCAAGCTAGACACTTAAATGAGTATGTTGCA  
AAATGGCAATTTCTTAGCACGGC

>Contig39

GACGTCCTAAAGAAATGCTAAGGTAACCTCAATTAATGCTAGAAAAGA  
GAGTTAAGTATTTAGGAGGATTTAATATGGTGTAAAGTTGTGAAAATCA  
AAATGGAGACACTAATGTTAAGAAAACCTGATAAATGGAGCCAGGGAAG  
GCCATGAAGAAAGAGTTCTCACACTTGATCCCTGATCATGAAAAAGACT  
CTGCAAAAAACAAACCTTGACAAAAGGCCATTGCAACCTTACACAAAAA  
ATACTACTTTAAAAGGACATGTGCCAGCAACTGCCTGTCCAACCTCAGA  
CTGGCAATATCTTTGTTATTGATCTTAGTAGCCAGCATAACTATTTCAA  
AACAGTGATGTAATGCTCATTTTTTTTCTTTTGAACCTTTTGTCTTCCT  
GTAAAAACCTTTGTCTTCTTTACTTACCCTGAATATGCACAGAGTTTACT  
ATGGAGTGCAATTTCTGTTGCAATGCTCTATTCCCAACAAACATCATT  
TTCTTTTAGAGAGCCTCTCTGTTTGTGATTTAGGTTGGTGATGTAAAG  
CAATGGCATAACTGAACACTGATTCAAAGAAAAGTGGCTTTTCTCTTGT  
TGTATTAAGAGAGGCCTTATAAATAGGATAGTAAGATTGTAAAGTTGAA

FIG. 4 (16 of 61)

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CTTAAAGCATGAAGAAAAATTTAGGGGCCAGGCAGGGTGGCTCACACCTGT  
AATCCAGCACTTTGGGAGGCCAAGACAGGAGGATTGCTTGAGCCCAGGA  
GTTCAAGACCAGTCTGGTCAACACAGACCTCATCTTTACTAAAAATAAAA  
AAATTAGGCCAGGTGCAGTGGCTCATGCCTGTAATCCCAGCACTTTGGGA  
GGCCAAGGGCGGAGGATCACTTGAGGTCAGGAGTTCGTGACCAGCCTGGT  
CAACACGATGAAACCCCATCTCTACTAAAAATACAAAAAATTAGCTGGG  
TGTGGTGGCGGCACCTGCAATCCCAGCTACTCGGGAGGCTTCAGGCAGG  
GGAATCACTTGAACCTGGGAGGCGGACATTGCAGTGAGCTGAGATAGTCC  
CACTGCACCTCCAGCCTGGGCGACTCAGCAAGACTCTGCCTCAAAAAAAA  
AAAAAAATTAGTCAGGTGTGGTAGCACACAGCTGTGGTCCCAGCTACTC  
GGGAGGCTGAGGTGGGAGGATCATCTGAGCCCAGGAGGTCAAGGCTGCGG  
TAAGAGCTGAGATTGTACTACTGCATTCCAGCAGGGCTACAAAGTGAGA  
CCCTGTCTCAAAAAAGAAAAAGAAAAAATTATGTTTTTAAATTTA  
TAATTATAATAAATTTAATTACATAAATTTAAGCTCAAGTAATTGTAAAT  
ATTCTTTCTGTGCACATAAGTTATTCTTGATTGACCCACAGGAGCTGG  
CCATTCTTCAAGTCAGAAGGCCTGAGAGAGGAGCTGCCAGGTGGTCTTC  
ATGGGGCTGTGCGGCCAGTCATCCCCACAGGTTGACAACTCCTTGTGTAC  
TTCATCCTCGTTGGATCCTCTGTATCCCTGACGATGAGCAACTGTGAGGC  
CCGTTTCAGCACTGAGTTCAGTCAGGAAAACATCCACCCACCCACCACA  
CGCTCACATTTACACACACATTACACATGCACACAGTTCTGGCTCCGA  
AAAAGAAAAAAAAGCAATTTAAAAATAATTCTGATCCTTTGCTTATTT  
CCACAACTCCATGAAAATTGTACATTGTCCAAGCAACATTTCTTAATAT  
TCTCTTTTTCTCTCATATCCATTTCTTACTGCTGTCTCCACCTTTCTC  
TTCCAACTCCCTGTTAAATCCCTGCCCCAGCGAATTTTATTCAATTT  
TGTGGAATGGAGGCTGCTCTGATTTAAATTAATAAAAAAAAAAAAAATCCC  
TACTCCATGTCCCAGATCCCTAGTTGTTTTTGTGTTTTGTTTTCTGAG  
ACAGGGTCTTGTGCTCTTCCATGCTGGAGTGCAGTGGCATGATCATGGCTC  
ACTGCAGCCTCAACCTCCTGGGCTCAAGTAAATCTCTTGCCTCAGCCCTC  
CCCAGTAGCTGGGAGTTCAGGTATGTGCTACCATGCCTAGCTAATTTTTT  
TCTTTTATTTTGTAGAGACACGGTCTTGCCAGGTTGCCAGGCTGGTATA  
GAACCCCTGGGCTTAAGTGATCCTCCTGCCTCGGCTTCCCAAAGTGCTGG  
GATTACAAGTGTGAGGCACTGCACCCAGGCTGGATCCCTGCATTTTACA  
GATTTAGCATCAAAAAGTCTAAACAATTAGACTGACTAAGGCAGAACTG  
CCCTTATGACAGCAGACATAAGAAGGAAAAGGCCAAAACACTGTGTTAAA  
AATTATCCAAATGTGAGGAAAAGGCCAAAGAGAGTAGGTGTGCCTTTTAG  
TGTCTAAGCTGCCTGCCCAAGGGGCATCTGATGCTCTCAGGCAGGAGTCC  
ACAAATTTTTTTTTGTAAAAGATCAGATAGTAAATCTTTTCAGCGTGAAG  
AGCATGAGGTCTCTGTACAAATACTCAACCACCATTAACATGAAAGC  
AGCCAACAGACAAACATGACAAATGAGTGTGGCTGTGTTCCAGTAAATC  
TTGATTACAAAAACAGGCAAGAGGCCAGAGCTGACCCATGGGCCATAGTT  
TGCTGACCCCTCTGTAAAGGAAAGTATTTTGTGTTGACTTGCTGTTTAC  
CATTTGATTGAACACAAAGGCTCTGTAGAGTTACTTGTAACTTGCAGAAGA  
TTGATGAGTGGCAAGTAATTTTTATTACACAGAATATANNATTATTCTGT  
TCAGTAGATAAGATAAACCCACTGTTATATTACTGTCTTGTTAGAATGT  
GACTTTGATTCATTTTTTACAAATTCATATTATTGCCCTAATTTGTATA  
TAAGTATGCTTCTTTTAAAAATATATATTTTAAATAAATTTGAGACAGG  
GTCTCACTAGGTTGCCAGCCTTTTGCTATAATGAGAGCATAAAGTGAAT  
TTCACACTTTAGCCTAGTGCATAGATGGGATTACAGGCACAAACCACTGC  
ATGCAGCTAACTTTGCTTCTCATTCCAGCACGTTCTATTCCNNNGNTTTT  
CATATACGCGTCTCTTAATGC

>Contig40

CGCATTACAGCCCAAGTTTTCTTCAGTGTTAAGGTTTTTGTGTTACTCTGTGC  
CCAAATGTCTTCCAAAAAGGTTAAGTTTTTTTACCTTCCTGCCAACATT  
ATATGAAAGTGTCACCTTTTGTAGACTTTTACCAATGCTGACTACTTTTG  
GTTTCAAAAAAGCTCTCAGTAATTTCTATTAATTACTTTTACCCTTTTT  
TATTGAGGGTGTCAACTTTTTATTGTTAGCATATTCTCTCTGGGCTCCA  
TTGGACGCCCTGGCAGCTTTTTGGTAGTAGGTGCCTTTAGAAAAGTCCTT  
CTCGTCTGGCCCTTTCTGAGCAAATCTAGTGAACAGAATTGGCTCCATGC  
TCAGCATTGCTTAATACGGTTGATCCAGGGCCTAGGACTCATTCTTCAT  
TACCATCCACTTGCATTGTCTTAAAGCAAGGCTCTATTAATTTAATTTGG

FIG. 4 (17 f 61)

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CATTTCCCTGTCCCAGCTCTTAGTTCATTAAACAAAGGCTTTAGAAAAC  
TCCAGTAGATGCCTATGTTGCTTCCTTTTAAAAAATTTTGGAGCTGTTT  
CCCTAGCCCTAACCTTTTCTTCAGGGCAGGAGTTAAGTCCCTTCTACTGCA  
TTCCCTGTGAAGATGGTGAATCAAGAGGCAGGGCACCTGTTGCTTTGTGAA  
ACAGTCCACTCTGCAGCTGGGCAGCTCTGTTACTAGAATGTTCTCCCTTC  
TGCGGAGCCCAATATTTTATGTCCTCTGTGAATCTCATCTGCTTATCCCA  
TCGTGTTTATGTCCTTGAAGATGCACAGGTCTGACACCACGAGGTAGCCCT  
TAGAAATTTGATGGCATTTCGATGTGTCCCCAACTCTTCTCCAACCACT  
CCTCCCAGAGCTTGTTTCTTAAGCCCCCTTGTTGGAGCTGATTGCTTTCCTC  
AAGGCAGCTCAGTTTTCCTCAGTTTGCTCCTGGTGGTCTGAAATATGAT  
TGACTCCTGAATACTCCAGGTGTGAAGGAGAGTGGGGGTGGCCTTTCTAC  
TTGTCATGGCCTGGGTTTAAAGTTGCTGTCCAGTGGAGCAGAGGTGACTT  
TCCCAGTGAATACTATTTTCCCCTCTAAATCCTTAGCAATTTTGTCTC  
CAGAGGCAAGACCTGGCCAAACCATTGTGTTGAGGATTGAATCAAGAAT  
GATTGAGGAGATGACAGTAGTCCCCCTCATCTGAGGAGGGCGTGTTC  
AGCCCCCTCAGTGAATGCCTGAAACTGTGGATAGTACCCAACTTATATGT  
CTATGATTTTCTATATAAATTAATACATGCCTGTGACAATGTTAATTTAT  
AAATTAGGCAAGAAAGAAATTAACAACAATAAGTAATGAAATAGA  
ACAATTCTAACCAATACTATAATAAAGTTGTATGAATGTGGTCTCTTT  
CTCAAAATTACCTTTTTTTTGGAGACAGGGTCTCACTTATTGCCCAGG  
CTGGAGTGCAGTGGCAGCATCACAGCTTACTGCTGCCTCGACCTCCTGGG  
ACCAAGTGATCCTCCCACTTTAGCCTCCTGAGTAGCTGGGACCACAGGCA  
TGCACCACTGTATCTGGATAATTTGTTTATTTTGTGAGAGAGAGG  
AGGTCTCACTATGTTTCCAGGCTGGTTTTGAATGCCTGGGCCCAAGGGA  
TCCTCCTGCCTTGGCCTCCCAAAGTATTGGGATTACAAGCGTGAGCCACC  
ATGCCTGCCCAAAATTTATCTTATTGTTCTATACCCACTCTTCTTCTGT  
GATGATGTGAGGTGATCCATTGCCTCCTTGATGAGATGAAGTGAGGTGAC  
TGATGTGGGCATAGTGATGCAGTGTTTAGGCTGATATTGGCCTGATGATA  
TGTCAGAAGGAGGGTCACTGCTTCGGTGATCCTGGATCATAGAGTCATG  
ATGATGTCAATGGTTGGATGTGAGGAGCAGACGATGTCAATGACTAACGA  
TAAGCTGGACAGGTGGGATGGTGGCACAAGATTTTATCACGCTACTCAGA  
ATGGAGCACAAATTAACCTTCTGAATTGTTTATTTTGGAAATTTTCAT  
TAATATTTTGGATTGAGTTGAGTTGACTGTGGGTAAGTGAAGTGTGAATGT  
GAGACTGTGGAAAGTGAGGGAGTACTGTATTATGGAAGTGAAGTCTAT  
TCGGTAGGGGAACAGAAATCACATTTGTGGGGCCAGGTCTCTGCATCTG  
TAGGGATCCAATTGTTTCATTCTCGTTGTAGCAAAACTTGGCTTTGGA  
ATCAGACAGATTGATGTTTGTATCATTTCTAAATGGGTGCAGCTACACTT  
TCCTCAAGAGGTAGTTCTGAAAATTTAACAAAATGTGAATTTCTTGGTAA  
AAAAAAAACCTCAAAAATATTCAGTTTCCTTCTTCTTGTGTCTGATGT  
ACTCCATCAAATACTGGGAAATATGTGTCTCTCATAGAAATGTCATGGAT  
CTTTGTAATTCGATTATCCACAAACCTTGGGGATTAGCTGTTTCAATGT  
TCCTATTTTACAGATAAGAAAATGGAGCCTGTGGTAAGTTAAGTGAGTTA  
CTCATGGCTACTTAACATAATTTTACTAGGTGATAGGCCAGAGCTAGAG  
CCCAGGTCACTTCTTATCAATGCTCTGCCTTGTCTCTGTGCCTTCCTGT  
CTGTCTGTATGTGTATGTGCCTGTTGACAGTAAGGCATAGTTTAAACCCAG  
TAGAACTACCGGTTTGTAAATGAATCCACTTGTAATGACTGACCATCA  
AGGAACAAGTGTTTTTCTATGCTTGACACCTGTTTGGATGCCAAAAG  
GATACAAATGTAACCTTCAGACACTCTGGGCCTCATTTTGCATCATTAGC  
ATGTCCAAAATTAAGAAAGACTGACCACACCAATATTGGTGAGGATGTGG  
AAGAACGGGAACCTTTCATACACTGCTGGTGGGGATGTAAAATGGTACAAT  
CCCTTTGGGTAAACAGTTTGACAGTTTCTTAAAAAGTTAGACATATATATT  
TACCATATGACTCAGCCCTTCCACTTCTAGGTCTTTACCCAAGAGAAATG  
AAATGCTGTGCTTTTACAAATGTCTATACAGGAATGTACATAGCAACCTT  
ATTTGTCATTGCAAAAACAGAGACAATTCACGTTGTCAAGAGTGAATG



GATGAGCAAGCTGTGGTCTCTATGCA...GGTATCCTACTCAGCCAG;  
AAAGATATGGCTAAT  
>Cont: g41  
GACAACAATGTCATGCATAAGATGACGATGGCCTGGGTGATTGATGCAAA  
CAAGGATAAAGAAAAATAATCAATTTTGTCCCCATTTTCAAAGACAGATAG  
CAGCAGCAAGAGTGTAAAGTCTGAGGAAAGTCATATTCCTTCCTCCTACAA  
CATAGCACACACACTTACAAAAACAATACACAGACTCCTGGCCAATGGAC  
TTCAAAACTGAGGAGGATCATTAATTTAAATGTTTACCGCTGCATGAAA  
TCTCCCTGGGTCTGCCCTCCCTTCCCCACCCTCCTCCACTTGGGCCCGG  
GCACAGCAGTGATTCTCTCACCTCTCAGAGTGAGCCAGTGTTGGCTGCAT  
TGAAGGCTCCAGATATGCAAAACAGGGCAGATATTCCTGGACCAGGTGCA  
CAGAGTGAGGCTCCAACGCAACCCTATTAAGTGCATGAAGGATGAATGAGC  
CTCTGGTATGGGCTGGGACAGAAAAAGGATTCAAGGGGCCCAAAGGGT  
TTGGGTGGAACCTACCAGGAGCGGCAGTACAGACTCCTTGGGAAGGTGGC  
CATGATTTAGCCACATTCACCAATAGGATAATCTGGAGAATTCCTAGCT  
TGAGTTTCTGGGAGAAAGCAGATTTCTGGATTATCTGGTGACAGGTAACA  
GGGCCGAGTTCATCCACAGCCACCTGCAGTGTTAGCACCTTAAGCTGAGT  
TCCTTGACCAGGATGCTGTACGCCCAGTCAGTGTGAGACGGTTCTTGG  
CTGAAGGCTGAAAAGCTTGGGTAAGTGACTTCACCTAAGCCTCTATCTC  
TTGCTCCCGTAAGTCAGGGCTCATTGTGGCTCCTTGACGGCTTGACTTCA  
GGGTAAACAGAGAAAATGAAGGTACAAGTGCCTTGTGAACTCTGAAACTC  
CAAACCAAGTCATTCTCAAAGTGCCGTCCACCAGTCTAGCACATCAGCATC  
ACTGGAAGCTTGTTTGAAATGTAAATTATCAGGTCCTCCAGAGCTATGTA  
TGAATTAGAACTCTGGGAATGGGGCCCTGCAATCTATTTCAACAGGTCC  
TCCAGGTGATTCTGATGCAAGTTAAAGCCTGAGAACTCTGTCTATACA  
AATGGATGTCAACTCAAGCTGCTCTTCAGAAATCACCTATAGCACTTGTTT  
ACCCGAATCCCTGAGAATGGAGCTTCAGGACTGCTATTTCTCAAAGTTTG  
CCTGGTGATCCTGAGATGGGGTTTGGGGGACAGAGATCCAAGGTGCTACC  
AGGTGTGAGGAATTGTTAGAAGGCAAACCTGGCTGTCTAGGGTGCTT  
AAAGGGTACAGATCCTAGGATTCTGCCTCTTACAGCTGAATCAGACTTTC  
CTAGAATGGGATTGCTGTCCAATGGCATGCCTCCTGGGTGACTCTGATGT  
ATAGCCTGGGCTGGGAACCAACAGAGGATTATCTTCCATTGACCAAGCTG  
ACAAACTCGCTTAAGGCTCTGAGTTTCACACTTGATTTTCTAGCCCCTGT  
CCTTCCATGGATCACCTGCCCCCTTCCCTCCTAATCAGGAGCACAGTCAG  
TGGATGCACTAATGTGGCCTCTCCTTGGCTGCAGGGAACAGGTGGAAATG  
TGGCCATAGGTGTGAGGGCTGCCTGCCATGTATTAATAGCTACAGATTT  
GAAAGATCCAAGGACAAGAGACTAGAAAAAATTTAAACAGCCAAGCAT  
TGGCCAGTAATGGCATTTCAGAAATCCACCAAAATATTAAGATGCTTTT  
TCAAAAAATATCCAGAGCACTCATGTAAAAGTGCTTAATTATTAATAAAG  
CTGACATGTGTGGTACTTCTGTGGGTCTGGCACTAGGCTAATTATGT  
TTTTAGGAGTTGACTCAAATGCTCCCTGTCAATATATGTGAAAAATAT  
AATTATTAGCTCCATGGTACAAATTAAGGAGAGGTTACATAAATAAAG  
GAATGATACTCAAATTAGTAACAGAGCCCATGCTCTTAAACACTATGCT  
ATTATTTGTGACTCTTACATAGGTGGCAAAAGTCAAAGGCTAGATTGAC  
TTCTGTCCACTTCCAGCCAAGATGAAGTACAAGATTCAGATACACCCTTC  
CGCATTAAACAACCTTAGGAATCAGACAAAATATACAAAGCATTGTTTGT  
ACACATTGGATAACAGACAGCACTAGATAGTCGTGTCTGAGAAAAGCGGT  
GAAATGAGCTGAGTCTTAGAATTGCCCCAGTTTACTAAGGGGCATAGTAA  
GGGCATAGCTGCAGCACAAAGAAGCAGAACCCAACAGAGACTGGCGTTCA  
CCTGAGTTGAGAAAACCAAGTTGAAAAATTTAGGAACACTAACACAGATAT  
GTAGGCAAGAGTATCAGAGAGGAGACAGTTGTAGGGAAAAAGAGAGCTTT  
ACAGAGAGACAGCGAGAGCTCCAGAGACCCGAGAAGATTGCCCTGACGT  
CACTAGCTGAGTACCGATCAGTGCATACATGTAAGGATATTACTCAATAT  
GTGAAAAGAACAGAAAGGAATGATGTCAAAGCTCACCCAAAGACAGGAA  
TCATTTATGTTTCCACCAGCCAGAGTGGAAACAACCTTGTAACGCATATGG  
AGTACTCAAACGAATATTTCTCAATAATAAGTTCAAATTAAGTGAAGT  
AAAGCCTGCCCGCTTGTCTGGACATGCCTAACAAAGCTTTGAGGGGAAGC  
CTCAAAAGAATGAAACCGTGTCCAAGTAATTTAACTGTGTCCAGAAAAA  
AATTCAAGAACATTTAAATAAATATTAATAATGATCAAACCCAGCAAGG  
TTAAATTCAAAATGTCTGGCATCCATTAAAAAATTACCAGCCTTGAAAAAT

FIG. 4 (19 of 61)

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TGGCGGGAAAATATTA: DATAATGAA .JAAAAAGCAATCAACAGA/  
AGGCCTAGAAAGTATACATATGATAAAATTAGCAGACATTAAATGGTTAT  
GATTAATTTATTTTATATGTTAAAGAAGGTAGAGAAGAGCATAAGCACAT  
TAAAGAGAGACAGGAAAGTCCCAGTACTCACACAGGGCCAGGAGCAGTTT  
TCACCAAGTCAGGTGGGAAAACCTTCATATTTTCATGGAGCATTGGTAGAGTA  
CACAGTGTCTTGCCTTAGTAGAGGGATAAATGCTGTTCTGTTCCCGCCTA  
ACCCATCTTGAAAGAAAATCTGAAAGGATCAAACGTATTCAAGTAACCT  
AATCACATCCCAGCACACAGCTCGACTAGTTATAAAAACACAAAATATTA  
ATATCTAGAAACACAAAATAATATCTAGCACCCAACAAGGTAAAATTCA  
CAATGTCTAGCATTCAATTGAAATTTTCTAGGCCATCAAAGAAGCAGTAA  
AATATGACCTATAAGGCCGGGCACATTGGCTCATGCCTGTAATCCCAGCA  
CTCTGGGAGGCCAAGGTGGGTGGCTCACCCGGAGGTCAGGAGTTCAAGAC  
CAGCCTGGTCAACATGGTGAGACCTCATCTCTACTAAAAATATAAAATT  
AGCCAGCATGGTGGTGGCGCCTGTAATCCCAGCTACTCAGGAGGTTGA  
GGCAGGAGAATCGCTTGAACCTGGGAGAAGGAGACCGCAGTGAGCCAAGA  
TGGCACCAATGCACTGCAGCCTCATTAGAGAACATCGGGAAG  
>Contig42  
GAAACTAAAGGCTTATTTAAAGCGCGAGACCGTGGCGCCTTTGGACTGGA  
CCCTTTCTAATGATCATTTAGTATCAGGCTATGTGGGAGTTGACCGTTTT  
GCATAGCCTGAAAGCCAACAGTATCACTCCTCCTCTAGGTGTGGCAGAGA  
TGTGAGAGAAGGAGACTGACAGTCTGTGGGTGTGTATGCAGTGTGGGGG  
AAGCGAGGCACAGGGGACATACTGTGGTGTAGAAAACCTAGTCTAAGGTA  
GCATCAGGAAATTCATGAAACCAAATGAATTTTATAACAGCACAAAGACA  
TTATTTGTTTTTGCCTCCCTCTCATTTTTTTTTTTTTTTTGAACAGAGTC  
TTGCTCTGTTCATCCATGCTCGTGTGCAGTGGTGCAATCTCGGCTCACTGC  
AACCTCCACCTCCAGGGTTCAAGCAATTCTCATGCCTCAGCCTCCTGAGT  
AGCTGATTACAGGTCTGCACCACCCCGCCGGCTAGTTTTTGTATTTTAG  
TAGAGATGGGCTTTTGTAAATGTTGGCCAGGCTGCCCTGTCATTTTTTTT  
TACTAGTGTCCAGTGAGTTTTTTAGGGGCTACATAACATGATACTGTCA  
TTAATCTAATGGCTAATGAAAGGGATATGTATATGTTTTTGTGTTTAAAA  
CAAACCTTCTTTGGGGTCCTCAATAATTTTAAAGAGTATAAAGGGTCCTG  
AGATCAAAGAGTTTGAGTTCTGCTGGACTGGGACAGTGGTTGTCAACCCA  
GATTGTACATTAGGGTCATCTGGGAAGCTTTAAAATAGTACTGATGCCCA  
ACCTTACCGCAAACCAATTAAGCCAGAATCTCTGTGGATGAGAAGTCTTC  
ATTGTATCATCACCATGACCATCATCATTGTACCGTCACTACACCATT  
ATCATCATCATCATCATCTTTCATTATCATTGTTAGTATCTCCATCACC  
ATCATCAGCATCACCATTATTATCATCATCATCATCCCCACCATCATCCT  
CATCGAACTTCACCTGCATGGAGGACAATCCACTATGCATTAGGTGCTA  
TGCTATTTGCTATACTCCTTATTCTCACAACCTGCCAGAGAGGCTGATAT  
TATCTCACTTTATAACAGGAGGAATCTGGATCGGAAAAGTTAAGGTAAGC  
TAATTCACAGAGCGAGAAGAGATAGAGCCAGGATTGAAAACCAAGTTCTCT  
GCTACATCAATGTTCCAGTCTTGCATATTGAGAACCTCTTTAGTTAT  
GCTTTCACCCCTCCAACACCACAGTAAATTTTTCTTTTTTTAAAAAAAT  
TATACTTTAAGTTATAGGGTATATGTGCATAATGTGCAGGTTTGTACAT  
ATGTATACATGTGCCATGTTGGTGTGCTGCACTATTAACTCGTCATTTA  
CATTAGGTATATCTTCTAATGCTATCCCTCCCGCTCTCCCCACCCCATG  
ACAGGCCCTGGTGTGTGATGTTCCCCACCCTGTGTCCAAGTGTTCTCATT  
GTTCAAGTTCCACCTATGAGTGAGAACATGTGGTGTGTTGGTTTTCTGTCC  
TTGTGATAGTTTGCTCAGAATGATGGTTTCCAGCTTCATCCACGTCCCTA  
CAAAGGATATGAACTCATCCTTTTTATGGCTGCATAGTATTCCATGGTG  
TATGTGTGCCACATTTTCTAATCCAGTCTATCATTGCTGGACATTTGGG  
TTGGTTCCAAGTCTTTGCTATTGTGAATAGTGCCACAGTGAACATTCATG  
TGATGTGTCTTTATAGCAGCATGATTTATAATCCTTTGGGTATATACCC  
AGTAATGGGATGGCTGGGTCAAATGGTATTTCTAGTTCTAGATCCTTGAG  
GAATTGCCACACTGTCTACCACAATGGTTGAATTAGTTTATAGCCCCACC  
AACAGTGTAAGCAATTCCTATTTCTCCACATCCTCTCCAGCACCTGTTG  
TTTCGTGACTTTTTAGTGATTGCCATTCTAACGGCACCACAGTAAATTT  
TTATAGATTTTATAAGCAAATTTGATTTTACTGTGCAAGAATTGGTTTATT  
TTTTAAACCATGTGTTGCAAACATACAATGGTTAATTGTGATATTTGCTC  
AGTACAAGATCATCAGATCACTACACAGACTTGAGGTAATTCACCTAAA

FIG. 4 (20 of 61)

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AGCAAAGAGAACTGACCCACATTAACTGAGAAGTCTTTACTTATTTA1  
CCCTATAAACGAGCCAATATGAAGAGAAGGCCTTAATGTGGTTAACTATG  
TAATTTTTTTCTGACTTTTTGAAATACTGAGAAGAGCTCATGACTCTCCC  
ATCTCCTAATTCTACCTFGGTGGATTTTAGACTGACCACAACTCATGGGT  
AAATGAGGGAAGACGAATAAGAAACCTTGCTTTTTTTCTCCTTGTTTT  
TGGCTGGCTGCAGTGGCTCACACCTGTAATCTCATCACTTTGGGAGGCCA  
AGGTGGGAAGATCACTTGAGCTCAGGATTTCAAACTGGCCTGGGCAACA  
TAGTGAGACCCCATCTCTAAAAAAGGCGACCG  
GCGGTGCGTGCTGTAATCCTACTCAAAAAGCCGAGGTGGAAAGAT  
CACTTGAGCATGGGAGGTCAAAGCTGCAGTGAACCTTGATTGCACCACTT  
CATTCAGCCTGGGTGACAAAGCAGGACGCTGCCTCAAAAAACAAAAAC  
AAAACCTTAATTTTTTGGCTATTCTTTCTGGTAAGAATGGTATAGAGAT  
GGGGATGAGGATGGCTATTGTATGAGAGAGCAAACAGGGTCCAAGCAGTG  
CTCTGGGCTGTCTAAGGACCAGTAGTCAGCTTAACTTCTCAAATTTCCAG  
GGAAGGAGTTCCGAGTGGTAGAATATCCTGGGTATGCCAAAGCATCACC  
TTGCAATAGCCTGTATGAATAATTTGTTTCATTTGTTATGACTGGAAA  
CTGGCTTTGTGTATGCCAGAGAATGGGGCAGGAAAGAGAGATTGGTGTCT  
TTGAGCTCTCTGCTGCTCTGGGGCAGTGATGCTTTCTCTCATGTGGAA  
GGAGAGCATGACTGAAAAGGTGCACAAATAAGGTGTCTGTGAGAGAAATT  
AACCTTCCAGATACAGAGACACAACCTTCCCCAAGAGGTCTCTATTGCTC  
TGCCTTTTTCTTTTTTTTGCTTGTCTACCATTAATAACAGAACTGA  
TTATGACCTCAAAAGAGAGGAGAAAGCGACTCTCCCCACCCTAGAGCTAG  
TTAACCCACATATCTTCTAGATCTCAGTTCAGAGTCACTTCCATCCCC  
AATAAAAGCCCTTGAGTGTCTGAGCACCTCTCCGTATAGCATTGTCTTA  
GGGGTTTTTGTACATTTTCTTGTGTGAACTTGGGTGACATCTGTATTT  
CCGACTAGATTACAGTTTCTCAAGGGTAGGGATGTCTTGCTTGCCATTT  
TCAGTTCAGCATCTAGACAGTACCTCAAGCAACAAGGCCGAGGGGGGT  
GCGGATCACGAGGTGAGGAGTTCGAGACCAGCCTGATGAACATGGTGAAA  
CCCCGTCTCTACTAAAAATATAAAATTAGCCAGGCGTGGTGGCAGGTGC  
CTGTAATTCAGCTACTCAGGAGTCTGAGGTAGGAGAATCGCTTGAACCC  
GGGAGGTGGAGGTGAGTGACCTGAGATCCACTGCCTCCAGCTTGGGT  
GACAGAGCAAGACTTCGTCTCAAAAAAAGAGAGAA  
AGAACATCAAAATGAATGAGTGAATGAGTGAATGAGTTAGCAGTGTGGA  
TTTAAGTGTGAGATTCTTCCCAGCTTGACTTTTTCTTTGGCTTAGTGAT  
TTTGAGGTCNCAAGATTTATTTTCTTTTCAAAAGGTGATCACTACCATA  
AGATCTTCAGAAAAGAAATGTGGCAAGCCANGTCTCACTAATGCAATCT  
CTATAACAACCTGTATCAGTACT

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GAGGTGTCATAAATATGGACCGATAGATGAATACAGGTAGGATGGGACAC  
AATCTAAGATCCCAGGGGGGGGAGACCACACGCTTGTTAGGGAGACCCA  
AAGTGGACCGTGTGGCCAGAAGAGTCCCGCACTGCACTCTAGTGACAGTG  
CAGAAAGTCACTGTGGGAAATCTAGAAGTTTCTACAGGTGCTATTTTAT  
CATAGCACTGTGCAGGCCAACCTTCTGCTCCACTGGCTGTTGGGAAAA  
GCTTTCTTTTTCTTCTAGCCAGGGAGCTCTCAAAGTGTTCACCTCTCT  
CACCTCCACCCAGGCGTCCAGGTGTGGAGGACACTTGCCGGCTGCTTGTC  
TGCTGACTCATCCCTTGTTTTCACTTGGAACCTACCACCAGCTGGCCT  
CTTCCAAGCATCAGCCTCCTCATTTTCTTAATCCCTTAGGTGTGATCTC  
ACCTCCACACAGTAGATTGCCTCAAGGCCCAATTCCAATATGAATAAAAA  
TGATTATTTTGTATCTTCCAATCTTCTTTTAAATATTATTTTATAAT  
TCCCTTTAGGAGGATCACCTAAGTGAAGACTATTTTACCTAAGAAATGT  
TAAATGTAAAGACATGGTTGTAATCTGGGGATTCTGTGTTAAATGGCTA  
GCAGACAGAAGTCAGACGACAGGCTAGAAATGTGTGAAGAGTGGTGCCT  
TTGAAAGGCGGAGTTGGTAATGATTTTCTTCCATTTTCCATGCTTTCCA  
ATTCTCTACAAAGGCCTTAATATTACTTCGATAACCAGGACCTCTGATAA  
CCTGCCCCCACCAGTAAAGACTTAGCTGGGAAAGTCAGCTTCATGTGAG  
GTAAAAGGAACAGGTAATACACAATTCCCACTGCCAAGTGTGGGTGTG  
CAGGCCTGAGCTTCTGCTGTGGGAGGAAAGAGAAAGAGAGAACT  
CCAAGATCCAAGAGATCCAGCAAGAAGGCTGGAGTCTGAGGACGCAGAAA  
GCTGAATGGCACAGTTACCCTATTGTGCTGAGGTCTGTGGCCTCTGGG  
TCTCTTGACAACCTGGGCAAAGACCCACAGAAAACCTATCTCTAGACCCTAC

FIG. 4 (21 of 61)

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CTGTGGGAGGGGAAAGTCTTCAGATCACTACAGGACAGCCACCTGGA  
CTCAAATGGCTTACAGTTCTTTCATCCAGAGGGTCTTCATCTAGTACATA  
CCAGGTGCTAAGCCTGGGTGCTGGAGACATGACGGGGAACCCATTTACCA  
TGGCTTTGTTACTGTGACATTACATCTAGGGAAAGCCAGCAAAGGGGAG  
GGATCGAGGAGAGCTTGTAGGCAGAGAAAATACCCAAGGGCAAGGGAGA  
AGCCAGCCTGTTCTGAGCACACACAGTGGTTCCATCTAACTGGGCCTCAG  
TGCCAGGTGGACTGGAGATGGGGCTGAGGAGCTGTACAGAGCATTCTG  
GACACAGATGTCACATAGTCCCTTGAGGTTAGGGTCTTAGGCATGGCAG  
CATTGCTTTGAGTTTTTCTTTTGTAAATGTTGCCATTATGACAATGTGG  
AAGATGGGTCTTGCAGAGAAGGGCAGGGCTGTGAGACCAGTTAGGAGAC  
TAAGATGTGAGCCAAGGAAAATGAGGAACACCTGAACACTGGGGCAGGTG  
CAGGGCCAGAGAGAAGCAGATGGCTTCTGAGGTTTTAAGTAGGTAGAA  
TCAAGGCAGCTGGTAAAGATCTTTATTACATATAAACTGGAATAAGCCA  
TCTGCTCCAAGACAAAAGAGTAGGCGGAAAACAATACAAGACAGAAATGG  
AATTAGAACAAACCTGGGAGGAATGTGGAATTAGAGTAGAGATCCAACA  
CTGGCTGCAATCATAAAAATGTAAAAACAAACAAAAATTTGCTAGGTGTGC  
TTACTTAGAAATAATTAGCTGTATATTAAGTTCACTTGTGTTATGGCTT  
AAATGTGTCCCCAAAATGTGATGTGTTGGAACTTGATCCCCAATGCAA  
CAGAGTTGAGAGATGGGACCTTTAAAAGGTGATTAGGTCATAAGGGTTCT  
GCCCTCATAAATGAATTAATACTGTTATCATGAGAGTAGATTCTTGATAA  
AAGGATGATCTCTGCCTCCTCCCCACAGCCCTCTTGTGCATGCTTTCTG  
CCTTTCCACCTCTGCTATGGGATGACACAGCAAGAAGGCCCTCACCAGA  
TGCAGCTCCTTGATCTTGGACTTTCCAGCCTCCAGAACTGTAAGCCAAAC  
AAATTTCTGTTTATTATAAATTACCCAGTCTCAGGTATTCTGTTCTAGAA  
GCACAAAATGGACTAAGATCATTAGATTATCATTTTTTATCAGACTGTTG  
AAGTGAAAAATAAAAAATCAAATAAAGAAATTAAGAGAGCTGCATGCAGCA  
GCTCATGCCTATAATCCCAGCACTTTGGGAGGCCAAGGCAGGTGGATTGC  
CTGAGCTCAGGAGTTTCAGACCAGCCTGGGCAACACGGTGAAACCCCTGTT  
TCTACTAAAAATACAAAAAACTAGGCCGGGCGCGGTGGCTCACGTCTGTAA  
TCCAGCACTTTGGGAGGCCGAGGCGGGTGGATCATGAGGTGAGGAGATC  
GAGACCATCCTGGCTAACAAGGTGAAACCCCGTCTCTACTAAAAATACAA  
AAAAAATTAGCCGGGCGCGGTGGCGGGCGCCTGTAGTCCAGCTACTCGG  
GAGGCTGAGGCAGGAGAATGGCGTGAAACCCGGAAGCGGAGCTTGCACT  
GAGCCGAGATTGCGCCACTGCAGTCCGCAGTCCCGCTGGGCGACAGAGC  
GAGACTCCGTCTCAAAAAAAAAAAAAAAAAACTAGCCAGGCATGGTGGTGT  
GTGCCTATAGTCCCAGCTACTTGGGAGGCTGAGGCAGGAGAATTGCTTGA  
ACCCAGGAGGTGGAGGTTGCAGTGAGCTGAGATCATACCACTGCACTCCA  
ATCCAGCCTGGGTGACAAAGCAAGACTACATTTCAAAAAAAAAAAGAAAG  
AAAAAGAAAAAAGAAAAAGAAAAAGAAATTAAGAGAAGGGCAGGTATTAA  
CCCCAAATATCCCACCATAGGGACACATTAAAGTTTGCTTGGCCACTCCC  
CTAGCATAATATATGGAATGTCTTCAAGGACCCTCTGTTGTAAATACAAG  
GCCCTGCTGGACTTAATACAACCTGCAGGCTTTGAGATCCCTACTCTGTT  
GCCATCTCTCATAGGATTTGCAGACCAAATCCAAATACTTAAAAATAGCAA  
CACTCACAAACATGCAAAATCAGAGCAGAAAAGAACTTCTAAAAGGCCCT  
GAAACTACACTTTATGAGAGAAGACAATAGGGACCTGAGGGTGGTAGAAT  
TTTCTCTCTATGCATCTATGTTTCCAGGGCTCACTTTCTCAATAAACTCT  
TAAATTGCTTTTAAAGTAAGGGAACAAGCAAACATTACATTTAAGAGAAA  
TCAATTTCATAAAGAAGGGGGGATGTCCAGGGTACTTTGCTTCCATGTTT  
TGCTTCCATGAATTTGTGTTTAAACAGAAGATGCAGAAAAACACACAATTA  
TTGCAAAATCAAGGAAATCCACTCTAAACATCCCTTGGTTTCCCAGGCCA  
GTGTACAACTGAAAACACATATTGTGGCTAATTATGTGTACAAAATTAG  
AATGACAAGGCAAGAAAAAAAACCTCTCTGATTAATAATAGCAGCCAA  
CACAGACAGCCTGTGTAGCTCGACTCTGCTGGTTTATAAAAGGCAGAAGA  
AGCAAACGGCTTCTGTGACCGCAACAGGAAGGGCCTCTGCTCTTAATAAA  
TAAATAACATTTAAATTATTCTCCCCATTTGCAAAGCATTTTCCAACCTC  
ATTATCTCATCTGACCAGGTATTATTGTATCTGACCAAGAACTGTATAC  
NAAATAAAGAAATAAAAAATAAATATGGGCCANGCACAGTGGCTCATGCTT  
GTAATCCCANCACTTTGGGAGGCCAGGCGGGTGGATCACTTGAGGTGAG  
TAGTTTGAGACCAGTCTGGCCGACATGGCGAAACCCCGTCTCTACTAAAA  
ATACAAAAATTAGCCCGCATGGTGGCACATGCCTGTAATCCCACTACT

FIG. 4 (22 f 61)

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TGGGAGGCTGAGGCACGAJAATTGCTTGAACTCGAGAGGCGGAGGTTGCA  
GTGAGCCGAGACTGCGGCCATTGCCCTCCAGCCTGGGCGATGAGAGCGAA  
ACTTCATCGAAAAAACAAAAACAAAAACAAAAACACCTTAGAAGA  
AGCGTTCCTCCTCTTGCTTTCTGAAGACACTCTACGCTGAAACAGTAACT  
TTCAATAAACCATCTCTTCTCACCACACTCTGCGACTTGCCCTGAATTCC  
TTTGTGTGCAAGATCCAATAAGCCTCTCTTGCGGTCTGGATGAGAACCCT  
TTTGTGGAATACTCTGACACAACAAATTGCAGAAAGAAAGTCTCACATG  
TATAAAATAAGCAAAAGATTCTCTGGCATCTGAAGAAACAATTTCTTG  
TCAATATTAGTATCACTATAAGTGTAGAACAACCTGTTGTATGATGCTAC  
ATAAAGTATATGAATCTGAATACTGTTGGATACAAAGGGAGACTATNNAA  
TGTAATACGTGCGCCGAAATGACTACACTGTTGGTGATCTTTCTTTCAAG  
AAGCANAAATTTGCCTCNAACATCCTGTACATGGTATAAAATTTTA  
>Cont1g44  
CCCAGCAAGAACACCAATACAACGGGGGGGGCGTTCTTTGTGAGGGGTGG  
GGAGGTCAATTTTTTGGAACTGCAGCAGGTAACACACAAAACCTTCCACA  
GCTGCTACCAGCTTTCCAGGAGAGCCTGTGTACCTGGAGAGGGAAGGCA  
AGTGCTTCCGAACCTTGACTTGATGTCTTAGATTCTGCAATGCGTAGTCTG  
TAGGGACAGGCTGTAGCTTATCCTATAGGCTTGGGCTGGAGTCAGCAAGC  
ATCTGGGCTGGCAGAGATAAAAGATGCAAAGGTGGAGGAAAGCATACGT  
GGTCTGGAAGACAGACTTGGTGGGTGGGTGGCTGCTACAACACCCCTAGTT  
AGAGGTAGAGGGGTAAGTCAGTGTGTCTTCTGCACAGGCCTCTTCCCCAC  
CTCATTCTTCATTTCCCATACAGCCTTGCTGAGTTATTACAAACATCTG  
ATTCAACTGGAAGCTGGGTTGAGGATGACCTAAAGGACTAGTGTGATGCC  
TGCCCAGGGGTGTGGGCCCATAGTCAGAGTCCAGAGCCTCCTCTCAGCTT  
TAGCACATCTCACCCACATCCTGGGTCCTTAATTAGCAATATGAAAGCA  
AGCCAAGTGACAAGATTTTGTCCCTGGGAAGTCCAGAAGCACTCCTTTTC  
TCATTTGTATAAGCATAATGATTTGCTTACATAAATAATCATGAAAATTC  
AAATCCCTCTCAGAAATCAGGTCATAAAACCATGAAATGCAGCATGTGGG  
CAAGAATCACAGGGAAAGGTAGGTCTTGAAAAGAAAGGATGGCAGGGAG  
GAAGAAAGCAGGGTGCCAGGGGCCCTGGGCTGCTGTCCAAGTCAGGTGGC  
TCACCGTCTCTGAGAACATTTCACTTTCTGGTAAATGGGGCAGTTGGAGA  
TAGAAGGGTTGGGTGAATGCCAAGAGTGAGCACAGCTGAGGTCACTGTG  
TGCCCTGCAGTCCAGGCGGGAGTAGAAATCCTGGGCCCATCTTACCTCCGA  
CCTCATTTCTCCTCTGTAAATAATGTGGGGGTGGGGGAAAGTTCTGGTCA  
TCAGCCCTAGCATTCCATGGTTCATTTCTCATCAGTGATGGAAAATCAC  
CAAGCAAGAGAACAGGATGGAGAATAACCGGATGGGTGCAATCGGAGGTG  
CTATTTTCAGGTGAGGTGGCCAGGGAAGGCCCTCTGAAAGGGTGGCTTGAG  
CAGGTGGCTGAATGTACAGAAGCTGCCAATCATGAAAGATCTGGGGTACA  
GCATGCCAAGCAGAGGAAATGCGAGTGCAAAGGCCCGAGATTGGATGTG  
GGCTTAGCACAAATGTGGCATGGCAAGAAGGCCAGTGTGGCTGAAGCAGC  
ATGAACAATGGGTGGAGGGGCTGAGAGGACAGAGGAGCAGGAAAGAGCCA  
GGCTTGGGTAGGAGAGGTGTCAACTTGATATATGATGCAAAGCCCTTGGA  
GGTTCCCAAACACAAAAGCAATGATCTAATATATGGTTTTAAAAATGCCA  
CTCTTGGCCCGGGCGCGGTGGCTCACGCCTGTAATCCACAGCACTTTGGGAG  
GCCCAGGCGGGTGATCATGAGGTGAGGAGATCGAGACCATCCTGGCTAA  
CAAGGTGAAACCCCGTCTCTACTAAAAATACAAAAAATTAGCCGGGCGCG  
GTGGCGGGCGCCTGTAGTCCAGCTACTCGGGAGGCTGAGGCAGGAGAAT  
GGCGTGAACCCGGGAGGCGGAGCTTGCAGTGAGCCGAGATTGCGCCACTG  
CAGTCCGCAGTCCGGCCTGGGCGACAGAGCGAGACTCCGTCTCAAAAAAA  
AAAAAATAAATAATGCCACTCTTGCTGTGAAAAATTGACCCTGGGGGA  
AGGAGGAGTAGAAATGTCAAAAGTGGAAGCAGACCACTCAGGAGGTCAGG  
GCAATGGACTGTGCAGGAGAGACTGACATCTTAGACTCGGGCAATAGGAG  
AGAAGGTGGTGAGGATTATATTCTGGGCATAAAGGCAACAGAACTAGCTG  
ATGGCGTCAACGTAGGAGATGAGGGAAGAAAGAAATCAAAGGGCATTCA  
TAGGTTTGAGGGTTGAGTAAGTGGGGATATTTAACAGAAATGGAGAAGTC  
TGGGGAAGGGGCAAGTATTGTGGGGGCAGGGGTCAAAGTTCTGTATTTT  
GGCCAAGTTAATTAATATTTGAGATACCTCTTAGGTGTCCAAGTGAAGAT  
GTCAAACAGTCAATTGAATACAAAATCTGAATCTTAGCCCAGGATGGTCT  
CACACCTGTAATCCACAGCACTTTGGGAGGCTGAGGTGAGAGGATCACTTG  
AGGCCAGGAGTTTGTGATCAGCCTGGGCAATAGAGCAAGACCCTGTCTCC

FIG. 4 (23 of 61)

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ACACACACACACACACA .AAAAAGTCAACAGGCATGGTGGCACATGCG...  
GTAGTCCCAGCTACTCAGGAAGCTGAGGCAGGAGGATCACTTGAGCCCAT  
GGTTCAAGGCTGCAGTGAGCTATAATCACATCACTCAATACTACACTCCA  
GCCTGGATGACAGAGAGAGACCTCATTTATTAATAAATAAAATTTAAAAAAA  
TTAATTAAAAATAAATCCAAATCTTTCCTGAGATTCAATTCAGGAGTAA  
CTGTCATGTAGAAGGCATATAATGCCATGGGTCACATGATACCATCTAAT  
GAATGCCACTGGAAAAGAGAGAATAGCTAAAAACTGAGCACTGGGCACAC  
CAGCAGCTGAGGTTGGAAGGAAGAAATGGAGCTAACAAAGGAGACAAAA  
GAGGAGTAGCCAGTGAGAAGAGAGAAACATCTGGAGAGAAGAGAGAGCAG  
CAAAAGGTGGGTGAAGGAGAATGTGGTCCACCAGGCCCAACAATGCTGAG  
CAGTTGAGTAAGTGAGGACCTGGCCACTGAATTTGGCAAGAAAGAGGATG  
TCAGCGGCCCTAGAACAAGGTGAAGAAGAGCTTGAGGACGGAAGCCTGA  
CAGGAGTGAAGTGAGGAGAGAATGAAAGGTGGAGACATGGAGCCAAGGAG  
CACTGAGACTCCCTTGAGTAGTTTTGCTGTAAAAATAAAAGTGAGTGCAGA  
GACGGGGCAGGGGACAGAGAAATGCAGGGGTAGCTGGAGGGAGCCACAG  
AATCAAAAGAGGGTTTTTGTGTTTAAGATGGTAGTTGTACATAGCACAT  
TAGTAAGTTCATGTGAATCACACGTTAGGTGAGACAGATCACTAATGCAG  
GAGTCAAATCCTTGACAGAGCCCCAGAGGAGGTGATGAAGGGAAGTGATG  
GACATCATTGAGATGCAAGTAGGTTAGCAATTCCTGGGGTACAAATAGGA  
GGTGACTCCTTTCTGATTGCTCCTGTTTTCTGAATGAGATAGCACATAAA  
GTCCACTCAGCCATGTGTAGCTGTTGAAGTCTTGTGGCTGTATGCCTGT  
ACAGACTGGGCTCTCTCTCCAGCATTTCTCTCAGACTAAGCTGAGCTG  
CACTAGCCGCTGCCACATCCTCTTGGGGCCATCCTCTGCCACACTCCACA  
TATTGCTGTGGTTTGCTTGCAACCCCTGGAAGGTCTACTGGCTGCTCCT  
AGAAGAGTCTGGGCGGCATCTCTCCCTTACTCGTTATCACATGGTGCTGT  
AAGCAGTGGCCACACACTTTAGCTGGTGGGATGGGCCATCACAGGCAGTA  
AATGCGAAAGACTGCTCAGATTTTAAAGCACCCATGAATCAGTAGAATGA  
GTTTAGAATTGTAGTCATCAACACACATTAAAAAAGGATTTAACTACAAC  
TAAAAAATAGTTGAGTAGGATAAAGCCATAAAAGATATTAACTACAAC  
CCAGATAGGAGGTGCAAAATTGTCCTTACATAAATCAGATGGAAAAAGTT  
GAAAGCAGATAAGATAAAATAGGTAAGCATGACATTTAAAAGGTATTCAT  
GGGACGTGGTTACAAAACCAACTCACAATAAAGTCTTAGGACCTCTC  
GCTGACTTAGGAGCCTGATCCCACTTTGAGAATGACTCAGTGTGTTACC  
CTGTGGCTAGTGTAGACCAATGATCCTGTCTCAGAGTCACTAGCCAACAG  
CCCATATCAAGTAATTGAACTTTGACTCAGAAACCTCAGTGTGAGAACC  
TTTGACTTAGGAACCACTGTAGTGGTTAACTGCAATTTGCACCCCTTAG  
TTCAGGGCTTTACAAACACCGGGGGCGGGGAGGGGGAAGGCATAGAGCTGA  
TGACCTAAAGGAAACCCATTGCAGCAACGCTTTTGTGTTAAGTTTACAAA  
TAAGTGTGTTTTAGAAATCCTCCAGGTAATGCCTTTGTTATTTAATGTGT  
CTGAGACAAATCTGCACATTAAAGAATATAAAATATTACCTTGTAATTCC  
AATTTGAAATGTGTAATTGACATTAGACTTCTATTTTAATTTGAAATGTC  
TAAACAATGTGGTTAAGTTTGTAAAAGGTGTGTGAATTTTGAGTCTGAT  
TTACTACATTTTTTTTTTAATTTTCTTTTTTTTTTGGAGTTTTAGGGATTGC  
TTAGATGGCTAGAAAGATCGCTAGGCACATGTCC

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GATGTGTGTACGTGTGTGCAAAATACCGTGCCTTTTTTGTGTTTTCTTTTGT  
GAAACAGAGTCTCACTCTGTGCGCCAGGCTAGAATGTAGTGGCGTGATGT  
CAGCTCACTGCAACCTCCGCCTCCAGGTTCCAGTGATTCTCCCGCCTCA  
GCCTCCCAAGTAACTGGGATTACAGGCGCCACCAACACGCCCAGCTAAT  
TTTTGTATTTTTTAGTAGAGACGGGTTTCACCATGTTGGCCAGGCTGGTC  
TCTAACTCCTGACCTCGAGATCCACCCACCTCGACCTCCCAAAGTGCTGG  
GATTACAGGCATGAGCCACCATGCCTGGCCAATACTGTGCCATTTTATTA  
TCAGGGACTTGAGCATCCATGGATTTTGGCATCCATAGGGGTCCTGTAAC  
CAATACTGCACAAATACCAAGGGACAACCTGTATTCTAAAAAGACCAAAAA  
TTAATAAGCAGGACGCTGAAGGTAATTGCCCAATAAAGTCATGATCCCT  
TGCCAGTGTCTGAACCTCAGCCAGTTTTCTACTCAGGACCTATTGGCT  
GCAGAGGTGGTAGGAACCATATGAGAATCTGCAATATCATGGCAAGTAT  
GCACTTTAATGATATCTGCAGTCTTCCCCAAAAGGACCTTACATTTACC  
ATACTGCTATGCTGCGTGAGAGGGTAATACTCAGATTTTTTTTTTTTTT  
TTTTTTTACACAACGTCTTACTGTGTTGCCACACTGGAGTGCACTGGCT

FIG. 4 (24 of 61)

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CGATCTTAGCTCACTGC .CTTCTGTTT .TGGGCTCAAGTGATTCTC:  
GCCTCAGTTTCCTGAGTAGCTGGGATTACAGGCGCCGCCACCATGCCTG  
GCTAATTTTTGTATTTTTAGTAGAGACGGAGTTTTGCCATGTTGGCCAGG  
CTGGTCTTGAACCTCTGACCTCATGTGATCCGCTGGCCTCCCAAAGTGCT  
GAGATTCCAGCGTGCGCGGCCATACCCGGCCGGGAATTCTTTATATATTC  
TGAAAACTAATCCTTTGTGAGACATAAGTGTTGTAAATATTGTATCCCAG  
TTTGTGGCATGTATTTTTAATTTTTAATGGTGTCTCTCAATGAAAAAAGC  
TTAACTTAAATGAGGTCAAATTGATCACCTTTTTATTATGGTTGATT  
CCTTTGGTGTCTGTTAGGTAAGGAATGTTGTTCTCTCCTGTCCCAAAGTTGC  
AAAGATTTCTTGTGTATTTTGTCTAAAAGTTTTAAAGTTTTGCTTTTCC  
CATCTGTGCACATTTACATTTGCTACATCTCACTGACTGCTTCCTCTGC  
TGCAGAGCAAGCTCCATGAGAGCAGGAGGCATGGGTCTGCTTCTTGTG  
GTCCCCAGAGCCCTATGTCTGACTAGGACCTGGCAGGGGACTAGTGAGT  
AGCTCCTGACTAACTGACTCAATGAATGAATGATTGGATGATTGAACAAA  
GTGGTATGGGAGTTACAGCGAGTAAGAGATGCCTTAGAAGAGATGAAGA  
AGGAGATGGTATAGGTAGTGGTTCTCAATTCGGGTCCATGGTGGACTC  
ACCTGGGGACCCCTAAAATGTACCGTGGAGGATCCCAGCCCAAGAGATTC  
TGTATGACTGGTCTAAGATGTGGTCTGGGCACCAGGTGATCCCAGTGTGC  
AGCCAGGCCTGAGGCCACTGGATTGGTGGTAAATGAGGTAACATCAAG  
GGTACAGACGTTGGTTGCCAACAGGCTTGGGCTTGAATTTAAGCTTTGTC  
ACTGACTTGCTGTGTCTCCTGCACTCGTTGAGCCTGTTTTCTCAGCTGA  
GAGATGGGTGTGATAACACCTACCTGCTGTAGTTGTTGTGAGAGTTAGAG  
GAGATAAGCATGTTTCTGGAATGAAGTGTGTTCTTAATCCATCATAGGTT  
TTTTGCTTGTGTTTGTGTTGTTGTTGTTGTTTTCTTTTCAAGAATGA  
GGTTGAGCCAGACTTTGACAGCTGGGTGGGAAGTGAACATGTGGTGATTG  
GGAGAGAAGGGCAGTTTATGTGAAGGGAATGTAATAATTAGAGAGTGGGC  
GTGGGAAGACATGCTGGGGAGAGTGAGCAGGCCGGTTAGCCCTGGTAGAG  
GGTGCAAGAGAGCAGTGCGGAATCTGCCAGGGAGACAGGTGGGTGACCAG  
GGTGCCAAAGGTGTGGCTTTTCCAGGTTCCCATGGACACAGCCATCCTC  
CCAGATGCCCCAGCCTAGCTGTGAGTGAGCAAGAGTTCTGGATTGTCTCTC  
TCACTCTGTCTTTTTCTCTCATTCCAGAAACAAAGCAGTGACTGGTACTT  
AGGAGGAGAATCAGGTCAAGTTGGGAGAACTTGCTTCTGCTCAGGGGAG  
CAGAAGCAAGAATGGAGGCCCCACCCATGCTGGAAGATGATGAGGGTTTT  
GGTTCAAGGGAGGAGGAATATTGGGGATCTAAAGGGGCCTGGGAGTGGGGC  
AGGACCCTGCCTTAGGACAGGTAGAAACATTTCTATAAAAAATGGGGTG  
GAGGTTGATGGTAGGACCAGGCATCTTTAGTTGGCTCCCTGGAGTGTCAA  
GCCCTTGAGATGGTCTTTAAAAGCCATGCAGTGGGGTTTGAATCTGGTGT  
TCAAGCTCATAGGTTATTAAACATAATGACACTTGGAACATTTTGGGAGA  
GCTCAAGTGAGTGGCCTGGAAGTTCTGTGTTGGTGCAGGAGGTGACTTAG  
GATGTGCTGCTCCAGACTCATATCTTTGACTGCACACCTGATGCTTCATC  
TGGCTATCCTGTAAGCACCTTCAACTTAACATGTCTACACAGAACTCTT  
GATATTCCTGTTCTCCCCAGTTCCTCAGTTCTTACCAAATGTTCTTCC  
AGTTACCCAATTGCTCAAGTAAAAAATCTAAGTCTTCTCTTGGATTCT  
GCCTGTTCCCTCAACATCCCACCTATCCATGAGTGTCTGTGGGCCCTGC  
CTCTGAAATAAATCCTGCCTTTGTCTCCAGTTCACTCCAGCCACCCATC  
CTGGGGCTGCACCCTCCTCCTTCCAAGCCCTCTCCCTTTCTTCTGCTG  
CTGCCTGTCTATGTCAAGCATATGCATCAGTGCGACCAGGACATTTGAAAT  
GCAACCAGTACAATTGGGCGCGGTTATGCCTACCAGTTTTCTTCTTAA  
ACATTTTATATTTATGTTTGAAAGCATGCCACCTTTCTTCACTTGCCAAC  
TTGACAGATTTATTAGTTGACAACATCCGCTGATAGCATCAGTAATAAGT  
TAATTGTTTTTGCACATGTAGCTTAAATTATTCTCATTATCATTTATAGG  
AGTTATTCTTTGTAAAGGGTAACTGAGTTTTCCAAAACAAACAGAAATTT  
GGGGTGGGCCCATGGAGCGTGACTCATGAAATCAGATTCTTAGAAGGACC  
TCGGCAAGTCTCTGGGTTGCTGTTAATGAGCCTGGCTGGCTGCCAGGGGT  
GTGTCTGCCCTTTATGAGGCCACCACTGTTCAAATGCTTGCCTGCAGCAT  
TACTTGCTAGGTAGTGCTTGTCTTACTGAACTGTGAGGATCCAATTC  
TTTGTGGTCTAAGTAACAATACTCAGATTCACAAGGAATTGATTAATAAG  
CCAGAATGCCAATGATTACATTTTGTATGAAGACCATATTTACAGTGAT  
TGATCTGCTCAAGCTCAAATTAGGATTAGAGTTCTGACAAATACATATG  
TGAGAAGTATGAGGTAAATACCTGAAATTTGGACTTTTCTAGAAAATCT

FIG. 4 (25 of 61)

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GAATGTGATTGCCATTACATACCTTTCTGGGGATGATGATTCTTGTA  
 TTTATTTTAAAGACATAGAAAATACTTAAGAATCAGATTGCTTGGCT  
 GGGCACAGTGGCTCATGCCTGTAATGCCAGCACTTTGGGAGGCCAAGGTG  
 AGTGGATTGCTTGAGCTCAGGAGTTTGAGATCAGCCTGGGCAACATGGTG  
 AAATCCCATCTCTACCAAAAATACAAAAAACAACCAAAA  
 AGAATAAATTAGCTAGGTGTGATGGTGCGTGCTTGTAGTTCCAGCTACTT  
 GGAGGATGAGGTGGAAGAATTGCTTGAGCCCAGGAGGTGGAGGTTTCAG  
 TGAGCTGGGGTTGCAACAGTGTACTCCAGCCTGGGCGATAGAGTGAGACT  
 CCGTCTCAAAAAAATAATCAGATTGCTTTATTGCTGGTTTTCTTTCT  
 AAAACTGAGATTGGGTCCCATCATCCCCTGGCCCCATTGGTTAATGGTT  
 CCTCCTTTGTCTATTGAATAAAATACAGATGTCTGCTTTTGGAACATGG  
 TTGAATGTAGACACTGCAGGGTCTTCCTGACTCAAAATGATTTAGGCTTA  
 GATAAAACACATTTGGAATGCATTTCTGGATTAAACCAAGGAAAGGAG  
 ATCTCTTTAAATCCCCTTTCTGTTCCCCCTCCCTACCCCTCCAATTGG  
 GCTTAAGTAAGAAGGGTGGTTACCCGCTAGTAAACCCCTTCGAAGGGGG  
 TCTTCTCCTCTAAGGGAAACCCCTTGTTTTGACATTTGCTTCAATGGGCC  
 CTTGTATTTTGTTCCTTGCTAAACGGGTGCTAAACCAGGGGCCTCCTCTT

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AAGGCTTTTAGAATATTTGCACACTTTAGAAATGGAAATGTTTTGGGGG  
 GCAGATTGTCTTAATATTTCTAGCTTGTGTGACATCCTTTTGA  
 AAGCAGCAATTCTGGCCTTTGTGAGAGATGGTGAATGCCTGCAGGTGTGT  
 GGACCAGTGCCTCCCTTCCTTACATGCACGGCCCCCAGCTGGGCCCCA  
 GCAGAGTGTGTACAGAATAATTTCCAAGGGCTGTGTCTTAACCTTTG  
 GTCTTGTCCCCCATTGCTGTAGATTGGCCAATTGACTTCATAAGTGCCT  
 CTTATGAACATAGATGTTGGCAATGGAAGTTGAGGACCAGTCAGTGGTTG  
 TTTTATTGAACACACAGCGTAAATCCCAACACAATGCTGACCTAAGAGAA  
 TTCCAGCCTCTGATTCTCAGTCTCTTTATATCTGAAAGGGTTCTGTTC  
 CACTTTTCCAGATCAAAATGTCCCTGCAGCTACTCAGCAGAGCTGTG  
 CAACTTATACGTAGAAGAGGTAACAGTCCACAAACAGAAAGGCACAGGAC  
 GAGAGTGGTCTGGGTGATGCTTCCTGTGGGGGAAAAGGTGATGAGGGTGC  
 ATCTGCACACCTATGTTCTAGGTAAGTCTGGGAGGAGGTGACCTCCCCT  
 TTGGTTGAGGTGCTGAGGCGTCTTGTTAGAATGGCACTATTCCATTTATC  
 TGATGCAGTCTGTGGGAATTTTGTGGTATGGCCACCACAGGTACCATGCT  
 GGGAAACAATGCCAGTACTGCCTGCTAAGCCACAGCATGAGTCACATGAG  
 CATTTGTGGGCTTTGGGAACTAAAGTTATTGAACGATAGTTATCTGAAAA  
 GGAATTTAGGGAAGGGGACTTTAGTCCAGCGAACAGTTTGCAAACCAGG  
 GGGAAAGGCAGCCTTCAGCGTAAATGAAGACGTGTGTGCCCCAAATAACA  
 AAGGGAGAGTTTGTCTTTTAGAGAGTAAATGTCCACGCAAGGTTCCACTT  
 AGGCAAATGAAAGATGCAAACCTTGCTTAGTTCTGATTGTTTACATTTGC  
 TGAATTCGGATTGGTCCGTGCAGGCTTTTCTGGGAACTCCAATACATGT  
 ATGACCTCTAGTCATACATGGCAAATGGCCGCTTGGCTCTAATTTGAATT  
 TAGGCCAGTTAGTCACTCAGGATTAACCTTTTTCAGGGTTACAGCTCT  
 GAACAATGGACTTAGACCTGCAGGACATAATCTGTTCTTAACCTCTGGGAC  
 TACCTGTGCCTTTTGACTGTGCCAGTGAGCAGCTGTGGCTCTGGGCCCCA  
 GACCCACAGGGCGATAAGGCACAGAGGTACGCATGGAGCAGGCTGTCTT  
 GCTGAGTGATCATGAAGATACACTTACATAGAGCAGCACTTTTCCTTCCA  
 GTCTTTGTGATTTAACTCATTAGATCCTTATAACAAGAGTCAGTCCTCTA  
 TTAAACCCATGAAGCACAGGTGGAGTCCAAGCTTAGTTTGTGAAGGATGA  
 GCCAAAAGGATTCTTCTTGTAGACCTCAAGCTCAGCTCTCTCCATGGG  
 CCCTGGAGTAGGTGAGAAGGCCTCTGTCTTCCAGAGCCCACTGCCAATCA  
 TCTACATTTTCTGTTAGCCCAATTCTAGGACATTGCTTTACCAACTGAAG  
 GGTGAGAACTATCATAAGTTATAAAAAATCAATTGAAAAACAAAAGGTAC  
 AGAACAGAAAATAAAGATGAGAATCTATTAAACATAGTGATGTTACTGG  
 AAAAGGGGTCTCAAACCAGACCCCAAGAGAGAGTCTTGGATTTACAC  
 AGGAAAGAACTCAAGGTGAGTTGCAGGGTGGGTGAATTGAGAGAGTTTA  
 TTGAAAGCTATTCCATTACAAAGTAGAGCATCCTCAGACAGCAAGTGGAG  
 GAACATGCCATCATTAAATTTTCTTATATAGGAATCTTGTCTATATAAA  
 GACTAAACTAAGCTGTGGCTATGTGTGGGTGGGCCGACAGCATGAAAACA  
 TTTATTCTCCTATTGATTTAAAGAGAACTATCCTTGACATTTTAGTGTGT

FIG. 4 (26 of 61)

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TTAAGTACATCAAAGCA1AACTATAATTA5CTTGAAAGCATATATTTT1A  
TAGGGATTGGGACATCTGGGCTTCTGTTGTTGTAGAAGTTTGTCTTGC  
AGGGATTACCAAGCCACTTCTTAGCTGTAAACATCTTAGGGCCATGGGT  
CCTGACTGGCAAGGAATGTGTCTTGTAGTTTTAAGATGGGCTTGATTG  
AAAATGGTGTCCATCTGGCTCTCCTAGGCTCCTGCTTCTTAACAGTAAG  
GGTAAATGCTATGTTATGAAATGTCATTTCTGCCTTTAGCTTGCAAACCTC  
TTGATGGTGAAATTCCTGTCCGTTTTTCAGTGGGGTATTTATTCTGCAT  
CCACGTCTTCACAAGGAGCTGAAAACAAATTGGATGGAAGCAACTGGGT  
TTATGGGACACGTTAATGTTTTAATGTCAATTTGGTGTGGAATTCAGATGT  
CCAAGCAACATTTTACACTACAAATCTGCAACTTTAATAATCACTCAAAG  
TACCTGAACCTCAATGCTTTCAGACAGACTTGGTATAAAGCCACCACCTC  
TTTCTATTATGGCAGCCCTATCCTGAGGACACAAATTTCTGCAGGGCTTC  
TGGCATATCTGTATTAAACAAATGTCAACAAGGTTAAACAAATGTCAT  
CTGTGATTTGTTTGTAAAGCCTGGATTTACTCATTTGAATATTTCACT  
CCTACTAGCATGTCTTGTAGTAGTTTTCTTCAGGGACCCTAATTATTGCT  
ATTAAAAATATGTGTGCAGCTACATGTTTTTTTTTTATCAATTTGCAATG  
AAAACCTTAATTGAATAATCTATTAGTGTTATTATTGAAAGTGAAATCT  
TTTCTTTTGCTTCTTGTCTCACACATAGTGCAGACAGTTTCCACACG  
GGCTCATAAAAGGAATGATTCTGCCTTGTGTGAACTTTTGCCTTTATTG  
TTAATTGCACCATTTTGTGACTGGCTTCTTGACCCTGTTGTAACCAAGCT  
CATAATGTACATTATTTCTTATTTTGCAGTTGTAGACACTTGAGGAAGTT  
CCCATTTCTTGTCTTCTTGTCTTGTTCCTGTGATAACTTTTTTCATG  
CAGACATTTTTTTTTTTTTTTTTTTTGTAGACCGAGTCTTGCTCTGTCTC  
CAGGCTGGAGTGCAGTGGCATGATCTTGGCTCACTGCAACCTCTGCCTCC  
CAGGTTCAAGAGATTCTCCTGCTTCAGCCTTTCTAGTAGCTAGGATTGCA  
GGCGTGCACTACCACACCCAGCTAAATTTTTCAAATTAGCCACCCACCT  
GGCTAATTTTTGTATTTTGTAGTAGAGACAGGGTTTCAACCATGTTGGCCA  
GGCTGGTCTCGACAGGTGATCCACCCGCTTAGCCTCGCATAGTTGCAG  
GTGCTATTCTGAGCTCAGGGCTCTGGCAGCTACAAGCCCAAGATGCGGTC  
TCCAACATGTGGCCATTCAATGTCTATGGCGCCCTCTACTGGTCTTGGGAA  
GCGCAGCTCTGCCAGTAGCTCCAGCAGGGCACAGCTGTTAAGTCGTGATG  
TTCTACAGGTGACCAAGGGCAATCTCTGGACTCCTTAGCCGCTAGGTCC  
TCTCTGTAGCAGGACCCAGGAGAAGGCAGGGGCTGAGGATGGCTCTCTTA  
GACATTTGTGATGAACCAACGTGTGCATTCTGAAACTTCTGTGAGCAA  
GCAGGTGAGTAGAGTTGGGTTATAAAAAAGTCTTAGGGTCTCACTACAGAG  
ATGGACTTGTGTGTAGATGGTGTGAGAGCCGCTGAAGAGTTCTACTTGGG  
GTAATGGTGTGATTGGGTTTGCCTTTTAGGAAGATTCTTGGCCAGAATG  
AGGCGGGCAACCCAGAGCAGGGAGTGGCCACATGTGGGTGTGCAGTTATG  
GGCCACTAATCCAGGTGATAAATGGTGTCTCTGAACCTCAGGTGGGGGTG  
CCACATGTCTCCATCTGCTCTGTACCCTTGAGACTGGCCTTATGGGCTGC  
CTTAGTGGTCTGTTGTCTCTATCTCCTGGTTGGGCTCAGGCAATGGGAG  
ATCAGAGGGAGGAAAGAGAGCTTGGTTAGAGTGACCCCGCCCCCTTCAG  
GTTGGCAGTGGCCACATTCCCCCTATACAGAAGGCCACAGTTTCTGTCACT  
GGCCCTCCACAGCCCCAGCTTTCTCAGTGGGCCAGCCACCTCCCCATCC  
CTTGCTCCTCCTCCTCCAGAGAGGGTTGTGGATTCTCACTGTCTCAGCAGTG  
CCTGGAGCTCCACCATCTCCTGCTGCTTCTCTGGACCTGCCTGCAGTTT  
TATAAATAACCTTCTTACATTACCTCTAGCATGCACCTTTTGTGTGTA  
TACTCTGCCCCCTGTCTAGCACATGACTCATGCCAAAGAGTTTGAATTTTT  
TTCTCCAGGCAACGGGAGGTCATTGGAGGATTTTAGACATTGAGAACAGA  
TGTGTATTGTGGAATATCTGTCTGACTGAAGTGACCAGGATGGTCCAAA  
AGAGCGAGAATTTGAGGCAAGCAAACCATCAGCAGGCCAGCAGCAGAAAT  
CCAGGTCATAAACAGGGAAGCTGAGGCTCACAGGGTTGGATCAGGGAATG  
GGAGAGGGAAGCCAAACAATTCCATGAGCATGTCACTTGCACATATGACT  
TGGTAACTATTTTTATTTTTATTTTTATGTTTTGAGACAGAGTCTCGCTC  
TGTCACACAGGCCAGAGTGTAGTGGCATGATCACAGCTCTCTGCAACCTC  
TGCCTCCTAGGTTCAAACAATTCTCCTGCCTCAACCTTCCAGGTAGCTGG  
GACTACAGGTGCGCACCCTACACCCAACTAAGTTGTGATTTTTAGTAG  
AGATGAGCATTACGCTGTTGCCTTAGACACGG  
>Contig47  
AATATTGATTATTTGACCAGAAATTCATGCAGCTAACCGTGACCCCTGGC

FIG. 4 (27 of 61)

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AAAATAAAATAGTGTAT...GTACGTGCATATACATGCAAAGAAATGAG...  
GAAACTAGAAAGGATGTCAATCAAATGATAACATGGTCATCTTGGGGTCGG  
AGTACATTTGGGGATGAGGGGAGCTGTAAAAGCAGACTTGGACCTTTTCT  
TCTACCAGTACCGTGTCTTTGAATTTTGGAAAGAAAAAAACTCAG  
AAGGAGGAGAAAGGAGCAGGAGGAGAAGAAGATGGATCTTAAGTGATTGTC  
CCGGGAGCACCTTGAGAAGGTGAGATTCAAGTCTAGGTCTAAGCTTTCTA  
ATTCCATGAGTGGGAGTGACCCACGTCCAAGAGGAAGCTCAAAGGAAGA  
TGTTCCTCCATCATCTCTTGCTCATCCTAACAGCATGCAAACCCACATCCA  
ATGCAGCTCAGAAAACCTCCCAAATTGCCAAATTTTCATTGGAAACACTTAA  
TGCTGTGGTTTCCAATTTCAACTGTAAAGTAGGTATGTATGCCATTGTTA  
CCATTAACTTCTCAGAAATGGAGAGAGCTCTCTTCCGCCTCCTCCCCCT  
CTGCTGTGGCTTTGGTGAGACGTGCACTCAGGCTCACCTGTCTCCATGAT  
CTCCAGTAAGTACACATGAGCAGAGAGGCCTCAGCTCAGCTCTTCTGGT  
CCCACCAGGGTTGATTCTTTGAGAAATTCTAGAATGCCACATCCTAGGCCC  
CCCAAGAAATCCTGCATCTTACCCCCAGAAATATGAATCATAGCAAATT  
TCAAATCAACCATCGTTTAATACTCACAGACTGGGCACATCCAAAAACAT  
ATTTTCAGTTTTACAACAGTGCCTGGTGCATATCGGCACTATTTGTGGAA  
GCAATAAATCGACACGGAGCTGAAACACAAACAAATGCCAAATTGTTTTT  
ATAACACCTGATTTTCTTCTGTTTCTTTATGCAGTTTAGTTTTGTTTTG  
CTTAACCTCTACCTCAGACCATAGTCTGGTAACTCACCACCAGAGCTC  
CCTTGAAATGTGGGTATGCAGCCACTAGGTGGCAGGAGAGAGTTTTCTGC  
CTGGAGGGAGGACAGCCACTCTGTCCCCGGGTGAGGCCAGGGCCACCCTG  
CTACCTGCAAAATTAGCATGGGGCTTTATGAACACAGCTTCCTAATAAA  
CACAGGATCTGTTTGATAGAGACTCCAAACACGCCTACCTAGTGATGAA  
AGACTCAACTTCAGAAGAAAACCTTCATGGCAAACATCTTCAGAGATGTT  
TCCAACCTTAAGGTTCTGAACACAGACGCTTCCCCAGAAAGCCATTGTTT  
TCAGCACCTGGGAGCCTTGCTTTGCTTTGCTTACAGACTCGCTGTTCTTA  
AATCACTGCCAAGATAACATCTGTCTCTTCTTACCCTCTATTTGATA  
TAAGGACTCCTCACTCTTGTTGCTTCTATTGGCTACCTCTCCACAGGGA  
GAAATCGCTGATTTAACAGCAGTCAATATCCCAAATCTGGAACAGGGAAC  
AGGGAAGCATTTAAAAATTGGAGAATTTAGGCCGGGCACAGTGGCTCATG  
CCTGTAATCTCAGCACTTTGGGAGGTGACGTGGATGGATCACTTAGGAG  
TTTCGAGACCAAGCTTGGGCAACATGGCGAAACCTCATCTTACAAAAAAA  
AAAAAAAAAAAAAAAAAAAAAAAAAACCCTAAATAGCCGGGCATGGTA  
GTGCACACCTGTGAGCCCCAGCTACTCAGGAGGCTGAGGTGGCAAGACTG  
CTTGAGCCCTGAGGTGAGGCTGCAGTGAGCCGAGATCACACCCTGCAC  
TTCAGCCTGGGCAACAGAGTGAGACCTTGTCCCAGATAAATAAATTAAAT  
TAATTTAATTAGAGGATTTAAGGATTTTCCCTACAGACACCTCCTTATTT  
TCTCTGGCCTTTTCTGACTACTCTCCCTAACTCCCTGCTCCTCTGGTCTC  
CCAAAACCTACTCCAGAAAAAAGGGGGGAGGGAATAAGGAAAGCC  
AGGTGACAGTGCCAGTGTGACAGATGACAAAGCATCTGCCCGAACAAACC  
GTAGGTCCCTGAACTTTCTCCAAGACCTGTCTGTGGACTTACCTATGAAA  
ACCAGTTTTAGCAAAAACCTCCTAAGCCAGTTTATCAAGATCCCCTTAT  
CCTCAATATCCATCTGATTGGATTCTTCAATCCCCCACCATTCCCAGTGA  
TGTCACCAGGCCTTTCTTCAGCAACAGTAGTTAGTGGGTGTAGCCAGGAC  
GCCCCCTCACCCCTGATATGCCCTTTTAGTAATTCTTCATCCACAGGTTT  
CCACCCTGCTCCTAGGCTATACATTCCCATTTGCCATGCTGCATTTCGGA  
ATTGAGCCCCAGTTCTATACTGAGGTCTTACTTCACCTCTCGCCATAGTCC  
TGAATAAAATTGGTTTTTCACATTTAAAACTGTCCAGCTCTGGTTGTTCC  
TTGACACAGGGTAATTTTATTCCATGTGATAGTTTGCCTTACCTCAGCC  
TACACCCCTCAAACCTGCAACTCTATATTCAAGAACCAGACAGCCCTTTC  
CAACAGATAGGAAGAGGCTGCCCTGGTGCAAAGGAAGAGGCTCTGGGAGG  
AAGGAGAGAACCCGAAGGCTGCCCCCTCCTCTAGACTGAGCTCTGGGATG  
GGTGGACGATAAAACCCAGATACGTTTAGACATCTGAGCGTGGAGAGGAC  
TTTGCTTTTGCTTCCACAGGGACCCCAAGGAACTGCAAGCCCTCCAGAGA  
CTAAAAACAGCAGAACAGCAAGAAATGGCAGCAAAGGTCTGGGCAGAATC  
ATCCTATGTGGGCACAGACACAAACAGAGTCCCCTGTGGCCCCAGGAGAG  
TTTAAAGAAGATCCAGAGGCTGTCTATTCCATATCTCAGCAGAGACAGG  
CCCGTGAGCCTAAAAGCTGATCATTAGGACAAGAAGGACACGAACTGTCC  
TGCAGCGTGAACCGCTGGAACAAGGCAATCACCAGACACCAGACCAGC

FIG. 4 (28 of 61)

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CAGACACAGCCCCGAGTCCCCAAGACCACCACGGACCCATCGCCCCCTC  
ACCAATAGCTCCAGGCTACATAGACCCCTCCACTTCATGGATGTCCTCA  
GAGCAGAAAGGGGAGGCAGGAGTGGAAACCCTGACTTGGTTTCAGTTGAAAC  
ATAAAATGACTGTACTATTATTGAATTGCTGAAGTTTACGTGAAAGAAAT  
GAGATTTAGTTTGGCCACAGTGCAAAATAAGAAACGAGGCTTCAACTG  
AGATTAAGGTGAGTTATAGGAAAATGTACTCCCTTGAAGGACCTGTGAAG  
TGTGTTGCTATGAGAAAATGACCAGAATCCACGTTCTTAGCTGCGGGAC  
TCAGGCTGACTCCTGTTTCTGGAGCTTGCACAAAGGGCAGGGAAATCCCT  
GTTTCAGGCACAGTGATTTCAATGTTTAAAGAAAACAGGTGGGCCCTGG  
CAATCATGATAACATGTCATAAGTTTACATCTCTGTGAGGCAGGTAGTGT  
AATCCCCATTTTGCAAAGGAGGAAACCGAGGCTGAAAGCAGCTACATGGT  
CTCTTCAATGTGGCCCAAATGTTGGAGAACAGAGCTTAAGTGAATCAGCA  
ATTCTATACTTAGAACTGACTCTCTCTTTATTATATCTCACTACTACCTT  
GATATTTGAAATATTCAACTTTTTTCAATCAAAAAATAACAATAATTTAG  
GCATAATGACTACTATGTCATTTAATTTCTTGCTGATATTTCAATATCCC  
ATGCCAGGAATATTGAAAGCTCAGCTCCTTAAGAGCTGACTATGGCATCA  
ACTCCCAACAACCATCCTTCCAGAAATATTTCCCTTTCTTTTGTTATA  
GAGTGGCACTGCCCTATATGGTGACCACTTGCCACATGTGGCTGTTGAAC  
ACTTGAAATTGGCTTGTGAGAATTGCAGTGTAAGTGTAAACACATACC  
AAATTTCAAAGACATGGCACATAATAAAAAATGTAAATATCTCATTAAC  
AATTTTATATTGACTGTGTAAGTAACATTTTGAATATATTGGATTAAAT  
ACATGGATGATGCCCCAACACCCACAGTCCCTTATCAAGTCTCTACTTCA  
CATTTTGTACTTCTGACTTAGAAATAGCACTGGCGTCTAAGAGCCTATT  
AATGTCGTCAATAGGTTCTTGGAACCAATTTTAAACAAAATGACATA  
TAAGAAAACGAATAACATTGAACAAAATGACATTATTCGAGGACCTGCTG  
CATGTTGTTTCACTTAAAGTCAGTGTCCAAGAACCTATCAGTGACATTTA  
GTGAGGACTTGTCTGCTTCTTCTGTTTACAGGAACCTGGGCAAGTTACTTA  
ATTCTCTAAGCCTGGTTTATATCCCTGCAAAGAGAGAAGGATAATAATC  
ACCAGTACTTAGTGATGTCGTAAGGAGAAAAATAAATAAATATGAAA  
TGGCTGACAGTGTCTTGTGACACAGAAGATGTGTGATCCACAGTAGCTG  
CTATTGTCTGCCTCACTTCACTAGTAATGGTCCAGGGAGGCCTTTAATGT  
GCATGGTGCAGTACATTACATGTTGGACATGGGTGAAGGGAAAGACCAG  
GCTCATCTAAACACAATAGGATGCTTGTGGTGTGTTTGAGGAGGAATCAAG  
GACTAGTTTATCCACAGCTGTAACATGCATGGATCAAAGAGATAAGGCAC  
ACAAAAGACTTTGTGAGTAGCAAAGCATTACAAAATGCAGAGACCAGCTG  
TGGGTGGTGGTGAAGTCAAGCCAGCTTCCCTCTGTGCCTGGCTGAGTGGT  
TCTGGGCAAGTCACGCCATCTGTCTTGATGCCCTTCCCATCTATAGAGA  
GGGAGCAACTGAGGCCCTTCCAATACTGAAGTCTTTATTTCTGCTACT  
TTAGAAATATCCACATTTTGGTAAATCAAATGATCCAATGATTCCATT  
TCCTAATGTTCAAAGTAGCCCCAGAAACATCTAAATGAATCAAACAAAT  
AAAATATTATTGTTGATGTTTGTGATTGCTGAACTTCTATTTTAGCAAC  
ACACACACACACACAGAACCCATAAGCCTTCATCTTTCCTTGATAAA  
CGAGCCTTCTGTCTGGCCATTTAAGTCACGATTAAGTAAATGATTTCCA  
ACTCGCCTTTTGCAGCAGTTTCAAGTGGGTCTTTCCTGCGTGGCAGTGGCC  
CTCCTGACTTATGATTTCTGTGTGTCGGCCTGTTACCACTGCAGCTTAA  
CTGAGGAAACAAGAACAAAACAGCTTCTGACCCCAAGAGACTGTTGGAGG  
CAAAGGCTTCAGTCCCAAGAACCTCACACGTGGGGAGCCCCGAGAGCCCAG  
CCCTGACCTTTTCTCCAGTAATAACATAAGAAACAACAGGCACTGGCCTT  
ATTTTGGATACAAAGAGTGGTGTCTTTCTTAAATCTTCTTTAGTCAGG  
GCTACCCCTTCATGGACGCCCCAACATCCATGGTTTCTGCTTGAGTCCCT  
GCTTCCATATTCTGCACTTCTCACTTGAAATATCCCTGGAGTACGTAA  
GCAGCCAGGTTTGAAGTTCTTGTGTGTCAGGCGGGTGTGTCATGTCCT  
CTCTCTCAACAGGACACAAGCTCCCCAAATCAGACGGTATGCCTCCACGC  
CCCTTCCCAAGCCTCCCGAGCAGCACCAGCATGTGAGGGGAGCTGGGGC  
CAGGCCATGATGGGAAGCACTCTCTGCTTAAAGACTAGGGTATGCGCC  
CTCAACTGTGGGAATGAGCCCCAGCTCTGGTGTCTGCCTCGGTTTTTCTCT  
CCTGGACAATCAACATGAACTCCTCACCCCTCTTATCCACTTTGCATAAA  
CTGAAAATAACAAACCCAGGGCTCTTCTGTGTCAGGAAAGGGTTTTTTT  
TTATAAAATTAACAGAGATGATTCAACACACCCAGGATATAACACATGG  
GCCATGAATCAAGGGCAGCATTGCTCTGGTCAGCCTGTTGTTTGGGCCCC

FIG. 4 (29 of 61)

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CTTGGCAGGGCTCTCCCLGAATCTTCCCCTCTTGACTCCCATCANACA  
GCACTCCANCTTTGTGTACAGGCGATAAATGGGAAAGGGGTAAAT  
>Contig48  
CATTCTTAATTAGAGAAACGCTCATTAACTAGACACCCAAATTCTCTGG  
GGGGGGATCATTCTTACAAGCATGCCCTTCTCTCTTAAAGAGAGAGCACT  
TTTTTCGCAAATAATGCTGCCATGAACATACGGGGTGCATGTATCTTCGT  
AATAGAATGATTCTATTTTGGGGGGTATGTACCCAGCAATAGGATTGCT  
GGGTCAAATGGTATTTCTGGTTCTAGATCTTCGAGATCTTCCACACCGTC  
TTCCACAATGGTTGAACTAATTCACATTCCTACCAACAGTGTGAAAGCAT  
TCCTATTTCTCTGCAACCTCGCCAGCACCTGTTATTTCTTGACTTTTTAA  
TAATCGTCATTCTGACTAGCATGAGAGACAGTATCTCGTTGAGGATTGA  
TGTGCATTTTGCTAATGATCAGTGATGTTGAGCTTTTTTTCATATGTTTT  
TTGGCTGCAAGAATGTCTTCTTTTGAGAAGTGTCTGTTTCATGTCCTTTC  
CCACTTTTTTAATGGGGGTTTGTTTTTTCTTGTAATTTGTTTAAGCTCCT  
TATAGACTCACAATAACAAAGACATGGGATCAACCTAAATGTCCATCAAT  
GATATAACGGATAAAGAAAATGTGGTACATATATACCATGGAATAGTATG  
CAGCCATAAAAAAGAATGGGATCATATCCTTTGAAAGGACATGGATGAGC  
TGGAAACCATGATCCTCAGCAAACCTATGCAAGAACAGAAAACAATTGTTG  
CATGCTCTCACTTATAAGTGGGAGCTGAACACTGAGAACACAGGGACACA  
GAGAGGGGAACAACACACATTTGGGGCCTGTGAGGGGTGAGGTGGGGGAG  
GGAGAGCATTAGGAAAAATAGCTAATGCATGCTGGGCTTAATACCTAGGT  
GATGGGTTGACAGGTGCAGCAAATCACTGTGGCACACATTTACCTATGTA  
ACAAACCTGCACATCCTGCACACGTACCCAGGACTTCAAATAAAGAGA  
GACAATACTTCTCCCTTAAGTGTCTACTGTTGCTTTGCAATAAAAAETTC  
CTGCCCTTCACTTCACTCTGACTTGTCCCTGAATTCTTCTCGTGATGGT  
GTCAAGAACGTGGACACTGGCTGGGGCTGGAGACTCACCAGCATCCGGAG  
ACCCTCCTGAGCCCTCCAGCAATACAACTTTGACACAACTATGAAATCA  
CAGATCCAAGAAGCTCAAAGAACCCAGCACAGGAAACATGATGAAACTA  
CATGAAGGAACATCAGAATTGAATTGTTCAAATCAGTGATAAAGAGTAA  
ATCTTAAAGCAACCAGAACAAAATATCCATCATATACGCAGAAATAAAG  
ATAAGTATGACAGCAGATTTACAAATAGAAAAAAAACAAGTGCAGCAAC  
AGAAACAAACTATCAATCCATAATTCTATACCTAGTGAAAATTTCTTTCA  
AAACAAAGGTGAAATAAAAAAATTATTTTCAGGAATACAAAAGCGAAAAA  
ATTAATCACTAGCATTTCATCACTGCAAGAAATGTTAAAGGAAGTCCTTTA  
GGCAGAAAGAAAATGATACAAGGTGAATATTTGGATCCCTGCAAGGAAC  
AAAAAGATCCAGAACTGATACTTAATGGGTAAACATGTAATTTTCATCA  
ACAAGTGAATGAATAAACAAATCATGATATATCCATATGATAGACTACTA  
CTTAGAATACAAAAGAAGAACTACTTATGCATGTGATAACATGAATGATA  
TTCAAATATTATTGAGTGAAAGACACCAGATCAAAACAAAGTACATAC  
TGTATGATTCTGTTTATATAAACTCTATAAATTGCATGCTCTTCTATAG  
TGACAGAAAGAAGATCAGTGGCTGCCTGCAGACAGGAAGAGATTACAAAC  
GGAAATGAGAATTCCTTAAGAGATGATGGACATGCTCATTACCCATCATA  
TGTATACAGCCATAATGGTTTTACAGATACATATATATGTACACGCCAAC  
ATAAATATAAGTTATCAAATTACAGTAAGTTCTGACTTAATGTCACTAGG  
TTCCTGGAACTTTGACTTTAAGCAAAATGATGTACAGTGAAACCAATTT  
TACCATAGGCTAATTGATATAAAGATGAGTTAGGTTTTTGGTTTTTTTT  
TTTTGACATGAAGTCTCGCTCTATCGCCAGGCAGGAGAAGAAGAGTTAG  
GTTTTACAGCATGTTTCTGGTCACAAGAACATCATCAAACTTGTAATAA  
AGGCACAAAACACTTCTAATATTAAATATCAAAATAAATATGAGTTATAC  
AGAATTTAAGAAAGATTAAATAAAAACAAGTAAATCATTATTTATGGGAT  
TTTTGGTAAATCAGTGAGTTATGTGGTCATAGTGGAAGTGGGTTAAGTCAA  
GAAATAAATGTTTGCAAAACAAAATTTTAAAGATCCTCTCCTACCACCA  
CACAAAAACAAGAAAACACGGTGGGCTCGCTAAGCACTTTTGTACCACT  
CGTATCTTATGCGTTTGTATGATTATTGTAATGCTTTATGATAATTTTT  
AGAGACAGGGTCTCACTCTGTGTCTCAGGCTGGAGTGAAAGTGGTGAATC  
ATAGCTCACTGCAGTCTCAACCTCCCGGATTCAAGAGATCCTCCCACCTC  
AGCCTCCAGTGTAGCTAGGACTACAGTTGTGTGCCACCATGCCATCTAT  
CTTCTTTTTTTTTTTTGTAGAGACAGGGGTTGTGCTTTGTTGCCAGGC  
TAGTCTTCAACTCCTGGGCTCAAGCAATCCTCCTGCCTCAGCCTCCCAA  
ATGCTGGGATTTGCGACATGAGCCAGCAGCACCTTGCCAGCATTTTTATT

FIG. 4 (30 of 61)

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TCATAATAATTATAAGTCATTCCCTTCATTTCATCTTACAACCCACTTGTTTC  
CAGTTTCAGGATCTCGGGTGACCAGAACCTATTAACGTTTCACGCACAAGTC  
AGAAACCAGCCCTGGACAGGACACCATCCTACCGCAGGGAGAACTTACAC  
ACCCACACTCACTCAGACTGGGACCATGCAAAGAACCTAACGTGCACTTT  
GGAATGTGTGTTCCATACCCACTAGAACAGCTAAAATTTAAAGACTGAC  
CATACTTGAGTGTTGAACAGGATGTGACACAATAATCTTTTAAGCGCT  
TCGCGTAAATGGCACAGCCGCTTTGGAAAACAGTTGGCAGTTTTTCAAG  
TTAAATATACCCAACTCTATGATCCACTTCTCAACAATCAAACAAGAGA  
AATAAAAGCAATGTCTACACAAAGATGTATACACAATGTTTCATTGCAGC  
CTTAATTATACTAGCCCCAAGTTGAAACAAGCCAAATGTCCATTACCAGA  
TGACTGGAACATACAAATTGTGGTATATTGATACAATGAAATACTACTTA  
GTAATAAAAAAGAAAGAGCTATTAACATAAGCAACAACATGGATGAATCT  
GAAAACAATTATGCTAAGTGAAAACAGCCACACAAAAGTTACATACTGTA  
TGATCACATCTACATAAAATTACAGAAAAGGCCAACTAATCTATAGACAG  
AAAAGCAGATGAGTGGTTACCTAGGGATGGGGCAGAAGGGACGAAAGGAT  
GGATTGCAAAATAGCACAAAATATTGGAGGGATGACAAATATATTTCATT  
ATCTTGATTGTGGGGATAGTTTAATGGGTATATATAGAGATCAAAGCTCA  
TCTAATTATACACTTTAAATATATGTATTTTCATTGTGCATCAGTTATTCA  
TCAACAAGACTATAAAATAATATATGCCTACATACATTTTTAAATATTCA  
AAATCTCACAGTTATATACATAAATGCAACTGAATATGTATTGAGATGTT  
TTAACAAGCAGAAAGGACTGATTAAACTCATGACAGCGGCTGTTTCTGGG  
AAGGGTGTAGGAGACAAGAGATGGAAAAGAGGATGAGAGCCAGAAGAGAC  
CCTTGTAATGTTTCCTTTCTTTTAGTAAAAATATATTGACAGTTAAAGCT  
GAGAGGTGAGAAATAAGTCTCATGGCTTTTGTGTCTTAAATTTTACA  
AACTAAGTGAAATGGGAGAAAGCAAAAAATAAACTTAAATAAATGTTAT  
ATTGCCCAAAAAGAGATTTAAATGGAGGTTAGACACATGAGACTTACGT  
TCTCAAAAAGTAGAATCTGCAGGGAAGTTTAACTATAAAGAATTAA  
AATCTAGCTTCTACCGCCCAAAGCCTAAATGTTCTGCTTTATTCTTCC  
TTATTATAATTCATAGGTAATATATTTTATGTTTGCAAATGAATGCAGTG  
ATATTAGATCTCTAAGAGGTGCTAAAAATGAAAAGTACATATTCCAATTT  
TTCCCAATTTTCTTCTCTTTCCATGAATGAAAAATATACATATTGATG  
ATTTCCAAGTTTATACAACCGATCTTTCTCTTAGTTTTCTCTTACCAAAT  
TCCCTCCCTCACTCAGCCACCAGCCAGTCCAAGTGTGCTACCTGCACAGC  
AGCCCTCATACCATCCACACTCTCATCAGGATCCTGCCTGACCTGCGAGG  
AGCCAGCAGCAAGGAGACAGAACCTCCAGCTGAGCATCTCAGGGCTT  
TCTCAGAGACTCCAGAGGACCCTGATAGGGACAGAGCCTGGCCAGCAATC  
CATGCTGCCAGCTGTATGATTGTGGGCATGTAAATTTCAACTGAAAATG  
GGTGTAATAATAACATGTTCTTCCAGAATGAGCTTTATGAAGATCATAT  
AGCTGTTTGGAACTCAGACAAGCACTGGTAGGAATACAAACAGGGGAGCC  
AACAGCCTATAAATAACTTTAAGAAAGGGCATGAATGTAATTACTTAG  
GAACAAAAGGCAAAGTGAGAGATGCCTAGGACTGAGCTGGACAAGCTGC  
ACCCTTTAGTGGCTCAGCCCATGGGCTGACAAGGAAAATGGAGGAGCTAC  
CAAAGAAGGTGGAAGGATTCTGGGAGAGTGGCCCTCACCCTGCCAGGGC  
AGGGCTCAGTGGGAGAGAGGGAGATCTGTTATAAATGCTGCCAGGAGGTC  
GAGTCATGTGAGAATGTCCATGTGAAAACATCCACTGTGTGTATCTAAAG  
AGAGTGGCTGTAAACAGGTGAGGGTCAAAGGTCTTATTGTCTCAGATGT  
TATCTGCATGCATTGTCTCAGCACAAGAAAACCTAAGGAGCATGGACACA  
AAGGGTTAGGTTGAAGCAAAAATTTAATAAGTGAAAGAAGAAGGCTCTCT  
CGAGTGGAGAGGGGAGTCTGAGTGGGTGCCACTTTGACAGCTGAATCCA  
AAAGCTTTTATAAGAACTCTTCTCATATCTGCAGCTGTTTGAGTAACTT  
CTCTTACCTATAAACTGTCTGTATAACTCTCCCTTATCTATGCAGCTGT  
GGGATGTCTCCAGGTAAGCATAAAGTGTAGCTTCTCTTGTGTGTATAACT  
GTGGGTTTGTGTTTAGGCAAGCCCCCATCCCTCCCTGTGTAAGCTCCCAT  
GGAGCCCACCATGTGCATATCTGAGAAGTGGAGGAAGCTTTCTCTGGGAG  
CTCACTGATCGTACAAAGAACAAGAGGCTTCTGTGCCGCTTATCTATTCA  
GGTGCAAGCTGAGTTTCTCCAGGCTGCTCTATTTTGCCTGTAGCTATG  
ATTTTTCAGGCAGGCTGCTTCTCTGAAGACTAGCCTTAACTGTCTACCTA  
TCAGATTTTCTTTTCTTCTCCCTCAGCTGGTTCCCTCACCAGGCTG  
AGCAAGTGAAAAGGAGGGCACAGGGCAGGCCAGTAGTGAGCAGCAACAAG  
GAACCTAAGACAGCAGAAACCACTCTTCACACCTGGGTTGAAAGGGGTGGG

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GAGCCAGGACTACAGC1 CAGGTAAGAACATAGGTAAAGAGATACTGTTGT  
TGTGTTGTTTTTAACTATGAGAAGCATTGAGCTTTAAATTTCTACAGGAA  
GGATCCAGTTTCAGACAGGAGCACCCTAATATTCAGAAGAGAAGAACATGGT  
GTAAAGGTCCTGGGAAGGCTGAGAGGATTGGGACTCAGAATCCAGAGCAG  
AAGCCGTCTGTGAACAGAAGAAGGACCTCCCCAGTGTAGCAAGAGGGAG  
GGAGGAGGGACAGATGCCAAGATGGTTCAGGAAGAAGGTTTGGTGGTAAA  
TGTGAGGCTGTGCTCACCTGCTGGCTTCAATTTTCTCTTTAAATGTCAG  
ATGGAATCATTTGATGAAGGCCATGCCATGCAATGAAATGGCAGTCTGAG  
GCATGGAGCAGCTCCAGCTTAGCCCGTGTCTTAGGGTAATTATGGCTCCAA  
CCCAGGAGATGAATATGACTAGGGAAAGTGAAGTCCAAAAACAAATGGTC  
TCAAGTTGACTGTGAGTCTTCTGGGAGGCTGAGACGACAGGTGGGGTTGA  
CAAGGGAAGGGGAACCCACCTGCTGAAAAACATCAGGCTGTTGGCTGGGG  
GAGGGGTGAGGCCCTGTGTTGTAGAGATGGATGGATGCCTAAAGTTGGGTA  
AAGGTTTCAACTCTACCCTCTGCTGGGTGTGAAATAAAACAAAGACCACC  
CAAATGAGAACAAACAAAGACTATTTATCCAGAGCTTGCTCTGACAAGGG  
AGTCGGCAACCATCACTTGCTTGGCAGAGACTCAGAAGTAAGCAGGGGAG  
AAAGCCTCATAGCAGAAAGAAGGGAAGTCTTCATGTATGCCCTGAGTGGC  
AGCTGTAGATGTGGGTGAGTTGCAGGTGGCTAACTAGAAATGGGGGACTC  
CTGTGTGATTGATTAGGAGCATGTTTGGCTTTCTCTGGTTGGTCCTACAT  
TGGAAGAGGGGAACAAAAAATTTAGGGCAGTTGTCAGTTATTAATCAAGTG  
TTGGCCATTTTGTACTGACTGTTACAGGAGTGAAGTGGCTCCCTGGATTGT  
TTGCTAGAAATAGTGGTCTTCACTTCTGCAAGTCTGACTTTCTGGTAAT  
AGGCTTCTGGGTGGCTATTGTGGATAATAAGTGGGTTTCTGAGCTGA  
TTTCTGCAGATTGTGGATCAGAGTTATTTTATATAAACAGTCTGACCATT  
TTCCACTGGCATATTTCCATCTTCCAAGAGCTGGCCAAGCTGCTGTCTTAT  
CTGTCTCCCCCAGCCCTCCACTCTGGCTGTGAAAAATACAAGCCACTAGG  
TGAGGAATGGGGACAATTGAAGACTGAAAGCTTTTCTTTGCTGGGTTTCGC  
AGAGCTGAGGAAAGAAATGACAACATCCAAGTGTCTGCCCTGGGCCAGTT  
TTAGGACTGTAGTGGTAATGCAAGGACTGTGTGAGTTTATATTTTCATTT  
GTCTCTCTAACTAAGGTGGAACAAAAAAGCAGAAAAATGTCTGTCTGCA  
GTCTCTGCAAAAGTCTAACACTGTGCTTCCCAACATTGCAGCCATTAGCC  
ACAGGTGAGTATCAAGCACTTTAAATGAGACTGGTCCAACTGAGATGTG  
CTCTGAGAAATAAACACACAGCAGATTTCAAAGACCTAGTACATGCCCTG  
ATTTCAAGCTATATTACAAAGCTGTGGTAATCAAAACAGTATGGCATTGG  
GAAAAAATAGACACATTGGTCAATGTGACAGAATAGAGAGCCCAGAAAT  
AAACCCGTGCATGTATAGTCAACTAATCTTTGACAAGAGTACCAAGAATA  
CACAATGGGGAAAGTCTCTTCAATAAGTGGTGTGGGAAAACCTAGATATC  
CACATGCAAAAGAAAGAAATTAGACCCCTGTATTACACAAAATCTAAAT  
TAATTCAAAATAGAAAAAGACTTACATGTAAGATCTAAAACCATAAAACT  
CCTAGAAGAAAACATAGGGAAAGAGCTCCTTGACACTGGCATTAGCAGTA  
ATTTTTCAGATATAACATCAAAAGTACAGGCAATGAAAGCAAAACAAGT  
GAGAGTATATCAAACTAAAAAGTTTCTGCACAGCATAAACAATCAACAGA  
GTAAAGACATGACGTATGGAATGAGAGAAAAATATTGACATCTGACAAAGG  
GTTAATATCCAAATATATAAGTAATTCACACAACCTCAGTAACAAAAGCC  
AAATAACCTGACTTTTTTTTTTAAATGGGCAAGTACCTGAATAGGTATTC  
CTCAAAAGCAAGATACAAATGGCCAAGAGATGTATGAAAAGCTGCTTAA  
CATACTAATCATCAGAGAAATACACAAATCAAAACAAGATATCATCTCA  
CACCTGTTAGAATGGCTATTATTAATAAATGAGATAAGTGTGGCCAGGT  
GTGGAGGAAAGGAAACCCCTGTACATTATTATAGGAATGTAAATTAGTA  
CAGCCATTATGGAGAACAGTATGGAGATTCCTTAACAAAATTAAAAATAG  
AATTACCATATGACCCAGCAATTCCACTTCAAGGAATACATTCAAATACT  
ATCAGTATCTCAATAAGATACTTGCACTCCTATGTTTCTGTCAGCGTTAT  
TCACCATATGCAAGATACAGAAACAAGTTAAATGTCCATCAACAGATAAA  
TGGATAAAGAAAATCAGGTACATATATATATACAATGGAATATTATTAG  
CAAAATCCTGACATCTGAGATAACCTGGATAAACCTGGAGGACATTATGC  
TAAGTAAATCAAAGCCTGACACAGAAAGACAAATACCACATAATCTCAC  
TTACATATGAAATATGAAAATGTTAATTTTATGGAAACAGAGTAGAATGG  
TAGTTGCCAGAGCCTGAGAGTAGAGAAAATGAGATGCTTGTCAAATCAAA  
TCATCACATTGAATATATATAATCTATTTGTCAATTAAATATTTTAAGAA  
TAAAAAATACCTGGCACCAAAAAAAGAAATGCAAAATGTCTCAACAATGTT

ATATGTATTGCATTTTG. AGTGATAATAATTTGAATATTAGGTTAAATAA  
AATATATTTGAAAAATTAACCTTCACCTATTTCTTCCATTTTGTAAACA  
TAGGTACAAAAAATTAATAATTACCTATGTGGCTCATGTAGGTGGCTC  
ACATTATACTTTGATGACACTATACAGGCTGGTGACCATATATCTCTTAG  
ACTAGTCTAAGTGATTTAACAGTGGTTCAGAAAGATCCAGGTTTAACAC  
CAATGAAAGGGCCAGCTGGCTTAGCCCAGCTTGTGTGGGAAATGTTGGGG  
AGTGGTTTAAAGACAGGGAAGCAAACTTTTGATGCTATTGACTTTTTG  
AAAAATCTTTTGTGGCTGAAAAACCAAACATTATT

>Contig49

GCTCGAGTGTGTCTCTAAAGCCTTTCCCCATTGGCTCCACTATACGCAC  
TCTCCTGGTTTCTCCTCCCTCTAGCCGCTGTCTTGGTCTCCTTTCTGATT  
TTGCTGCGTCTCTGTCCCCTGAATGATTGCTTCTCCACTACGGGTGAT  
TTTGCTCCCCAGGGACATTTGGCAATATCTGGAGAGGTCTATGGTTGTG  
TTTGAGGGTGTGCTACTGCCATCTAGTGGGGAGAGGCTAAAGATGCTGT  
TAATGCCCAGGACAGTCCCCATAACACAGAATTATTGAGCTCAAAATATC  
CATGGTGCCAAGATCAAGAAACCTGCTCAAATATTAGCATGTGCTGAAG  
GCCCTTCTCTTCTTTAGCAATATCTGCCTCCTTAGGGATCTTTTCTAG  
TCTCAGTGGTTTAAACATTTAAATCCCAAATTAGGCAATAAATTGGGCCC  
CAAACCTTCGTTAGTATAAAATGTAGAACTGTGTTATTAGAAGGCTAATAA  
AATGACCTGGTGAGCATCTGCAGCTAGCCTCTGAGCAATTCTGGGGACCA  
CGTGCAAGATAAATCCATCTGTTCCCTCTCTGTAATGTGGCGCTACCTTG  
TGGCCGATTTTCTCCTCGGGTTAAATATCTCTGGGGATGCAACTGTCTG  
GTTAATGGCTGTGTGAGGCCAGCGCTGGTGATAAAGGAATCAATCAAGA  
CAATATTGAATTTAGAAAGGCAGATTTATTTAGAGAAAAGGAGAGATACG  
TTGCAAGGGAGCAATGGGCAATACAGCAGAGGGAAGGCTGTCTGCAAAGA  
GGCAAGGGCTACGTATGACGTAGGGCTGCTTAGGCTGAATGCTTGCAGAC  
AAGATGCTTGCCTGTCAGGTGGGCTGTGAGCTGAGTGCTTGGGTGCTAGTG  
AGCCATTGGCAGCTGACCCTATTTCTTGAACATTCGCTCCCTGCAAGCA  
TTTTAATGTTAAACCGCCAGGTGAGTTTGAATTTCTTTTTTCTTTTTT  
TTTTTTTTTTTTTGCCTTTAGTAGGACCTGCCGTTGTGAGACTATCTGAGG  
TAAATTAGACACCCTCCTGGTTTAAAGTCACCGCTCCAGTGACTAGGCAGG  
GAGCTCTTCTTGAAGAGGGTGTGGGCAGTGGGTACTTTGCATGTTGTCC  
ACACCAGGCGAGCTGCTGCTTCAAGGCTTTGCAATTTGCTCTTTTCTTTG  
CCCAAATGCACCTCTCTCACTGTTACATGATTTTTCTCCCTCTTTTCC  
TTTAGTCTTTGCTTAAATATCACCTTCTAGGGAGGCCTTCCACACCAC  
CTCTTCAAGATTTGAGGGTATGCACCCCCACCCCTAGCCTTCTTATCCCT  
CTCCACTGCTTTCTCTCAAAGCACTTGTTACGTTCAAATAAAATAGATT  
AGTTACTTTATAGTTCTAATTTTACTATTTTGTGTTACTTCATCAATAC  
CCATGTAATCTCTGGAAGGAACGTTTCTTTTGTAGTGATTTCTAGCAC  
CTAGAACAGTACTTGGCACATGGCAGGTGTTCAAAGTATTTGTTGATTA  
TTTTCTCAAAGGCATGGAGTCTTAGAAGTTTGAGAACACAGTTCTAAGC  
ACAGCTGTTTAGAGACTATGGATGATGCTAATGGCTGTATTCCAGTAGG  
TGGGGCAATTCTCAAATTGACCTGGAATCCTTGAGATCTGGGGACAGTCA  
CCAAGCACTGGGCTCTGTGGGGAGAGATGTGCTGGTTTTTAGAGAGGAGA  
ATAGCATCCTGGGGGACTTGGCCCCAGGGCTTCTCTGTCCCAATCTCTTC  
CCAACTGAGTCCAGAGGCAGGAGGCTTGTCTGTAGCTGGTCAGTCCTG  
TAAGTGTTCCTCCCATCTACACAGATGCAAAGAAGGCTGAGAAAAGCA  
AGCTGTCAAGGTGAGCAGGGGCCCTGACTCCTCCCCAGAAGGCACTCAGAA  
CTTCCATAGGGCAACTGGAAGAAGGTTCTACTTCTCACCGGCAGCTGT  
TGCTGGGGAAAAAACAGCCTCAGGCCCTACCCTGTGCTGAGAACCTGAA  
TCCAGTATCAGGTTCTCCAACAACTTGGATCCAGCTGACCCTCACAAGG  
GGTCAGATGCAACCTTGTAGCATATGGAATGGAAGGCAAGGTCCTTGTG  
TGGACTATGCCTAGAATCTAAATTAAGACAAGGCCTCAGAGGGGCTAAGT  
GACATCTGTCTCAAAGTTTTCACAGCTAGTGTGTGACTAAATCTTGATT  
CACCTCTCAGGTTTTACCATATCCCAAAAAGGTTGAAACAAGAAAAG  
TTATCTTTGGGCAATTACCTCTTTCTGTTCTTGTCTTACCTACTAATGT  
TCTAGGCTCACCTCTGGTCTGCAATCTCACTGAAGTACAGATCCCTCA  
TGGCCTAAAGGGTTTTCACTGAGGTTGACTAGGCTCTCCATTGCCTGT  
CCTACTGTCTAAGGCACCTCCTGGGTAGGGTGCCAGCGTCATTCTGATG  
CTGCCTGACTTCTCTCCAGCTACTTTTGAACCTTGGTATCCATGGCAGA

FIG. 4 (33 of 61)

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FIG. 4 (34 of 61)



TCCAGCGGTGATTGGG .TACTTTTGGGAGGCTGAAGCGGGTGATTTC  
TGAGCTCAGGAATTCAGACCAGCCTGGTCAACACGGTGAACCCCTATCT  
CTACTAAAAACAAAAAATTAGCCGGGCATGGTGGCAGGCGCCTATAATC  
CCAGCTACTTTGGGAGGCTGAGGCAGGAGAATCGCTTGAACCCAGGAGGCG  
GATGTTGTCTAGCTGCTGAGATCGCGCCATTGCACTCAAGCCAGGGCAAGA  
ATAACAAGACTCTGTCTCACAACAACAGCGAACATACGAAACAAACGT  
AACATCCAACTAGCAGGTACAGCTGCCGTGCCAGTCACTGACCCATGGTCTAT  
AAGATGTCTACAGCTCAGGAAGCAGCTGCACATGCTGTACATAGACAAAC  
TCTTATGAAAGCAGAATGTCTGTATGTCTCCATAACACATAACAGTGTAT  
GCTTTTATTATGGTCACTACTCTAGCTGTGATGTACCTACGCTCTAATATG  
CCAACGATAGTTTTCTTTAAATCATCAACATAATAAATGTATGCTGTCA  
GTCCCCCACATGTAGACATAACTTAGCTGGTACATGGATAAGAAACCTAT  
ATTAGATAACCTTAGGCCAGGTGTGGTGGCTCATGCCTGTAATCCCAGCA  
CTTTGGGAGGCCGAAGCGGGTGGATCAGCAGGTGAGGAGATCGAGACCA  
CCCTGGCTAACACAGTGAACCCCGTCTCTACTAAAAATACAAAAAAA  
TTAACCGGGCATGGTGGCAGGCACCTGTGGTCCCAGCTACTCAGGAAGCT  
GAGGCGGGAGAATGGCGTGAACCCAGGAGGCGGAGGTTGCAGTAAGCCGA  
GATCACACCACTGCACTCCAGCCTGGGGGACAGAGCGCAAGATTTCTGTCT  
CCCAACCCAAAAANCNANNNNAAATTTGCACCCAAATCTGACTAATTCCA  
GAGCCAATTCGAATTTAGAATCGTTATATCTCCCTGGTGAACCTGAAGCTT  
TTATCTTTAAGGAGACACACTCTTTATGTCTACCAATGCTTATTGECTTA  
AAGTCCACTTTGTGCAGATACAGCTGCTTTCTTTAATTAGTTTATTGTGTG  
GTATATCTCTTTCCATCCTTTTTCTTTGACGCTTCTCCATTCTTACATTT  
TAGATATATTTCTTTTTTCTTTTTTTTTTTGAGAGAGAGTCTCACTCTCTC  
GCCAGGCTGGAGTAGTGCAATGGCGCGATCTTAGCTCACTGCAACCTCC  
ACCTCCTGGGTTCAAGCAATTTCTCTGCTCAGCCTCCCAAGTAGCTGGG  
ATTACAGGAGCCCACCACCAAGCCCAGCTAATTTGTTGTATTTTTAGAAG  
AGATGAGGTTTCGCCATGTTGGCCAGGCTGGTCTCGAACTCCTGACCTCA  
GGTCACTCCACCACCTCGGCTTTCCCAAAGTGTGGTATTACAGGCGCGA  
GCCACCATGCCAGCTGATTTTAGCTGTATCTCAAAAACAGCATGGGTTCT  
TGTTTGCTTTCCTTATTAGCTTTATAATGTAAATCATTTACATCAAACA  
TCTAATACACCATGGACTGTAAAAACACAGCCATATTTTATGTATGAATTA  
AAAAAAAAAACACCACCAATTAGTTCCTGAGACACACACCTTAACAATAT  
CTCTGTGATGTGCATAAATCAATCACATCAGTTTCTCTGCACCTCAAAAT  
TTCTTTCCTCAATTTCTCAGAGATATGGCAATTTCTCTGGTTTTACATTCC  
CAGAAGCAAGAAAAAGTACACAGCTTCTTCAAGTCATGATGACTCTTT  
TTTTATAGCTCTTGGTGTTTTGCAAAAAAGATTTGGAATTTGCTTCACTAATA  
CTAAATTTTCATTCTGCTGCTCTGTTTCTATGACAAGTCAGAGGGCATCT  
TTTTGAAGACATTCTAAACAGCAATTAACCTCAAAACATGTAATGACAAT  
GACACACAAAACCTCAACTGATGACCAAATGAAGAGTTCAGCCAAAGTTGA  
CACAAGCTGGCTGACAGAGCTTGTAATACACACAGCTTGGCATATGCCTC  
GCCATTTAGAGATGTAAAAATAGGAATAAATGTTTTCCCTTAAATCAAT  
GAAATAGAGCATTTGGACTGAAAATCTACGACAGTTATAGTGTTTTCTAT  
TCATTATTCTCATCTGTTTTCTTCTCCCTCTGCTTTCTTTTAGTTTGAA  
TATTTTCTATCATTTTCATTTTTCTTCTCTACTAGTTTGAACCTTATGCATT  
TATTTTCTATTTTTAGCACTTACCTAAATTAAGTCTGTAATCCATGGAT  
CCTTAATTTATTTAAAAAACTAATGTTAATGAGTAGCTTTATTTTCTCTC  
CATCTAATTTAAGGCCACAGAACACCTTCACTTACCTCAATCCTCTCCC  
AAGTTACATGCTTTTAAATGTATATATGTTAATACCGTATACCTTTTAAA  
CTTTCTAAAAAGCATTATTTTATAGCATGAGTGTTCAATTACATTTTGTG  
CATATATTTAGAATTTTCTTTGCTCTCTGTTTCTTCTTCTATTTATGACT  
CCCCCTGGGATCAATTTCTCTCTACTTGAAGTACATAGTTTGAAGCTGC  
ACTATTCAATACAGTAGCCACTAGCCATGTGTAGCTATTGAAGTTTAAAC  
TAAGTAAATTTAGTAATATTTAAAAAACTCAGTTCTTTCATCTCACTAGCC  
ACATTTCAAGTGCTCAGCAGCCACATGTGACTAATGACTACTGTACAGCA  
AACATATAGAACATTTCCATCATGGCAAAGAGCTCTATTGATAGTGTTCA  
TCCAGAGTTTCTGTTCCAGGACCAAACCTGAGGGTTGGGCTGCTATTTCTC  
ATGGCCCAATAACAAGATGCAGATGAGCTGGGGAGGAAGAGGTTTTAT  
TTCTGCAACCAGTATACAGGGGAAGGCGTGGAAATCATCACCAGGCCAAC  
TCAAAATTTAGCTGTTTTCCAGAGCTTATATACCTTCTAAGCTATATGTC

**FIG. 4 (35 of 61)**

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TACGTGTAAGTGTGCATLACCTGAAGACGTAAGTGATTAACCTCTTTTAA  
ATCTGTAACCTAAGGTCTGAGTCCGGAAGATCTTCCCCTGGAGCCTCAGTA  
AATTTACTTAATCTAAATGGGTCCAGGTGCTGGGGTAATTACCCTTATCT  
TGTCCCCTGCTAAATCATGGAGGTTTGGGGAATTCCTTTAGAGCACCAT  
TAACCTGTTTGTGAAGGCCTGGGAATTCCTCCAAACCCCCATTAAACC  
TGTTTAAATCCCAAATTGGTTCGGTAAAAAATTCCTCCTTAATTTGTCCA  
ATTTTAAAGGCCCAAAAAGGCTGGGGCAAACCTCTGAATGGCCTTTGTT  
ACATTCCAACCTTTGTTTAAAAACACCGGTTTTTAATATTTAACTTAACC  
ATTTAATCTCTACTGAAACACTTGTTATATAAATCTGCATTAATGAGAAC  
TGGCCTGCGCCATATCTCCTTCTCAGAATATCTTAGGGTTGTGATCCCCT  
GTGTGAAGAGAATATATCTCTGGAGATCTCAATCTCTCTACCCCAAAAAA  
AATCTCACTCGGAGAAAACCTCAGACTCTTATCTCCACAGCGCTATCTCTC  
TCCTCTCC  
>Contig50  
GCTTGTCTAAGATGGTGTCTCCTTGTTGCTGTGCCTGCTTTCATCCTGGGA  
TCTCCCTTCACCATCAGGATTGCCTTCACCTCATTCCAGTCTTGGATCTT  
TCTTCTTGTTTCTTGAGTATTTTTTTTTTTTTTTTGTCTGCATTCCCTTCA  
GTGGCCTCTTGGGAAAAGATGTGTAGGGAGAAAAATTTCTTTAGAACT  
TGCATATCTGACAATATATTTATCCTATCCTGACATTTGGTAGATAGTTC  
AGCTGGGTACAGAATCTAATTAATTTTCTTCTGATTTATAAGACATT  
GCTCCATTTTCTTCTGGCTTCCAATATTGCTGCTGAGAAGTCTGACACCA  
TTCAAATGCCTGATTTTTTCCATGTGATTGTTGTTTCTGTCTGGAGTGT  
TGTAAGATTGCCTCTTTATCTACAGTGTCTGAAATTTTCATGACGTAGGT  
CTTTCTTCATTCAATTATGGTAGACACTCAGTGGGCCATTTAATCGGGAAA  
AACATGTGTTCTTCAAGTTCTACAACTTTATTACTTCTTTTTCTTGTTG  
TCTTCTCTGGTCTGTTTTTCAAGCCCGAGTCTCTTAGATCTGTCTCTAA  
TATCCTATTGACTTTACTTCATTTTCTAAGTCTTTATCCTTTTGCTTTA  
CTTCCGAGAGACCTGCTTAACCTTATCTCCCACTCTTTTATTGAATTT  
CATTTCTTTTACTATATTTTTTACTTTGAATACACCTCTCTCTTCTCCTC  
ACATTTTCCCCCATAGTATTTTGTCTTCAATTGACAGTTCTACTATCTTA  
TTACTCTGGAGATATTAATAAGTTTTTAAATTTTTATTATTTTTATT  
TTCAAAACAGTGTCTTACTCTGTCACTCAGGCTGGAGTGCAGTGGTGTGA  
TCATGGATCACTGCAGCCTTGATCTCTGAGCTCAAGCTATCCTCCTGCTT  
CAGCCTCCCAAGTAGCTGGAACCAAGGCATGTGTCAACATACCCAGCTA  
ATTTTTTTGTTTTTGAGGTGGAGTCTCACTCTGTAGCCCGGTCTGGAGTG  
CAGTGGTGCAATCTGGGCTCACAGCAACCTCTGCCTCCTGGGTCTGGTT  
CAAGCAATTCTCCTGCCTCAGCCTCCTGAGTAGCTGGGATTACAGAAACA  
CACTACCATGCCAGCTAATTTTTGTATTTTTGTAGAGACAGGTTTCACC  
ATGTTGGGCAGCCTGGGTCTGAACTCCTGACTTGTGATCTGCCCACTTGG  
GCTCCCCAAAGTGTGGGATTACAGGCGTGAGCCACTGCACCCGGCCACT  
AATTTTAAATTGTTAATAAGACGAGGTCTTGCTATGTTGCCCAGTATG  
GTCTTGAACCTCGTGGGCTTAAGTAATCTTCTGCCTCAGCCTCCCAAAGTG  
TTGGGATTACAGGTGTGAGCCACTGAATCTGACATTTTTTAAAGTTTTT  
TTCTCTTTACCAAGTCTTTTTTCCCCTTTCTGCTTTTTTGGGTTGTTTTA  
TTTTGATCTCTATCTTGCTAGAACTTTCTGGAGACGTTTAGTAATACTA  
GATTTTTTGAGAGTGGGCACTGGAAAGCTGATTGGAACTCTGAATACAT  
GGGTGAGGCTTGTGGCTGTGAGTGTCAATTGCTTGATGTCTGGCAAGGC  
CAATGGGTTTGGGACCCCTACTATTAGTATAGGCCTGATTCCTGGGAAA  
GGCTCTTTTGATCTCCTGCCTGGAGGATAAAGGCCTGGCTACCAGCCTTC  
TGTGTGTAATGTGAGGGAGAAGGGCTGGAGTATTCAACATCATGCTGAAT  
CCTTTCAATGATCATCTTGTTTTTTAGTAATCTCCTACCTTAACCTCTCTGT  
CTTCTGCTAGTATGGGAAAGATGACCTGAAAATCTAACCATTTATTTTC  
CCCCATTAATATCATTTTATGATTATTGAGAAGTTAAATAATTGTGATGC  
TGTCTTCCAAAAAGACTGAATCAACTAGCAACAAATAAGAATTTCTCAC  
AGCTCTGCCAGCATTTTAAAGAATAGCTTTATTGAGCCCAGGAGGTCAA  
GGCTGCAGTGAGCTGTGATTACACCACTCTACCCAGCCTGGGTGACAGA  
GCAAAACCTGTCTCAAAAAGAAATTTAAGGAACAGCTTTATTGTTGTA  
AAATAGACATACAATAAACAGAGCACATATTTAAATTGTGCAACTTATAC  
TTTGATATAACCCTGTGAAAACATCACCACAATCAAGATAGTGAATATAT  
TTATCACCTCCTGATACAGTTTAGCTCTGTGTCCCCACCTAAGTCTCATG

FIG. 4 (36 of 61)

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TTGAATTGTAATCCCCAATGCTGGGGGAGGGGCTTTGTGGGAGGTGAT1G  
AATTGTGGGGGTGCACCTTCCCCCTTGCTGTTCTTGAGATAGTGAATGAGC  
TCTCATGAGCTCCCCCTTCACTCACTCTCTTCTGCTGCCATGTGAGGAT  
GTGCTTGCCTCTTCTTTGCCCTTCTGCCATGATGTGTTTCTGAGTCCTC  
CCTAACCATGCCTCCTGTACAGCTTGCAGAACTGTGAGTCAGTTAAATCT  
CTTTTCTTCATAAAATTACCCAGTCTCAGGTGGCTCTTTATAGCAGTGTGA  
AAAGGAACATAATATACCTCCTAAGTTACCTCAAGCTTCTTCTTAATTCCT  
TCTCCTCCCTTCTTCAATTGCCAAGCAAACAACCACCTGTTTTCTGTAC  
TATAGATTAGTTTACATTTTGTGGGTTTTTTTTTTTTTTTGTAGACAAGGTC  
TCACTCTGTTGCCCAGGATGGAGTGCAGTGGTGGCATCATAGCTCATTGC  
AGCCTTGAACCTCTAGTTTCAAGTGGTCTCCCACTTCAGCCTCCTGAGT  
ACCTGGGACTACAGGGGTACACCACCACAACCTGGCTTAAAAAATTTTTTA  
AATAAAAAATGGGTCTTTGTTATGTTTCTCAGGCTGGTCTCGAACTCCTCG  
CCTCAAGCAGCCCTCCCTCCTTGGCCTCCCAAATTTGTTGGGATTACAGGC  
ATGAGTCATGACTCCTGGCCTAGTTTACATTTTCTAGAGTTTTGTATAAA  
TGGAACATACAGAATGTATTTTTTGGCGAGTGGGGGAGTGTTCTATT  
TCTTTCTTTCTTTTTCTTTTTTTTTTTTTTTTTTGTAGACGGAGTCTCG  
CTCTGTCTGTTGCCCAGGCTGGAGTGCAGTGGTGGCATCTCGGCTCACCG  
CAAGCTCCACCTCCCGGGTTCAAGCAATTCTCCTGCCTCAGCCTCCTGAG  
TAGCTGGGACTACAGGCGCCCGCCACCACACCTGGCTAATTTTTTTTGT  
TTTTTGGTAGACGGGGTTTCCACATGTTAGCCAGGATGGTCTCGATCT  
CCTGACCTCGTGATCTGCCCGCTTCGGCCTCCCTAAGTGCTGGGATTACA  
GGCGTGAGCCACCGTGCCCGGCCCAAGTGTCTATTCTTAACCAGCTT  
TCATGCAATCTTTTTTATTTTACCATCTCTGTGATCCCACTCCCAAAGG  
TACTAGATGTGATTTGGTCTTAGGATCAGCTACCATTTGCCCAACTGCT  
TTCCAGCCTTCCAAAAATTTTTTCTTTTTTCTTAAAGATACTCCTGTG  
TGAGGCTCAGAACTCTGAATTGCTACTGCAAATATGAACCTGGTGATGT  
GAATGCCAGGGAATTGCTGATTGATCAAAGAAATGTATCCCTTCTCCC  
TCACTCTTGCTGTCTTCTCATTTGTTTTCCCCATCCTTGTGGATTCTGTA  
ATTTAAATATCCCTTTAATGTTATAATATTTAATGGCGTTTGGCGAAAA  
GTACAGAATTAGGTGCAAGAGTGCATAGCTGTTATTTTTTTTTTGGCCTC  
TGAGACTGTTCATATATGCAAGTTATTTAACAGAAAGTTCTGCAGTGACC  
TGAGATGTGAGGGGGTCTGATAGAGTACGTTTGAAGGCAGTTACTGGAA  
AAAAATAATGCCATTTCTGGTTTGTACTTCGGTAAGTTCAGATGACCCAA  
TATATTGTTTATGCTGAGGAGTTCAGTAAAAAAGTAGCTTCCCTTCTCTT  
CTTCTTCTTTTCTCCTTTCTGCTTCTATAAAGCATCTGCTTTGGGAAA  
CTTCTTAGGAGGAGAGCTTGCCAGCCCGTGGGTAATGGAGAGGTCTTGCA  
GAGATAAAAGAGATGCTCCCACTCAATGCAGGATGGTGTGGAGGTAAATG  
GGGATACGTCTGGCATCACTCAGGAATGGGCCTTCTGGCAGGGAAGAGA  
AGGGAGGGGAAAGAGGAAGGGAGTCAAAGATGAATTGCTGAATACGGGGGA  
TTCCAGGGCTTGAGCCAGGAAGAGAACTTTGGGAGGTGTGAACCTGGAG  
GGCATGCTGATGAGGAGCAGCCTGAAGTCCGGGGAGGACCTGTTTTTG  
GTGGCCAGGAAGAAAGTGCCTTCCACACACAGGGAGGCCACAAGGCTGAT  
GGGCTGGGGGTGGAAGGACAGCCCTAGGACAGGCTTGGGAAGCAGGCTC  
AGGTAGGGACTGCGAGGTTCTTGTTGAGTCTTTTTCATTCCTGGTCTTAG  
AAAATAGAAATCCAAGGCCTCTTGAGAGTGGAAAGTGGGTGGGAGGAGGG  
CAGATGGGGCTTAGGCCAGGACACCCGTAGAGCTACTGCCAGCTGTCT  
CTCAGGGACTCTGCTGAGGTCACTCCAAGGATCATTCCTAGCCTTGCTAG  
ACAGTACTACAGAGGGAACCGTAGTATCGCACCCACTTCTTCTCTTTC  
AATGAAAGTTTAAAGGTCACCATTTCTCTGGCAAAGGAAGTTCCACAAA  
TATTCATTTCCGGTCTTAGAAACAGCAAGGTATCAAGCAATTGCAAAC  
TCCTGTGCTGGGGAATTCCCAAGGAAGTAGGGGCAGAGTTCTGGTGGAGA  
CAAAGTGAATTCCGAGTGATTAGTCAGTAGCAGTAGCAGTAGCAGTAGCA  
GTAGCAGTAGCAGTAGCAGTAGCAGTAGCAGTAGCAGTAGCAGTAGCAGC  
AGCAGAACCAGAAATTTCCCGCACGTGTCTCAGGCTCTCATTTGCCAACT  
CAGTCTCTAAGTATTTTTTATTGGCAGGAAAAATAAAATAGCTATGAGTGA  
AATAATTCATTAGACCTGAGCCTCCATCAATTTTGTGTTTAAAGGCCTGA  
CTCTCTTTACCTTTCCCTGGGATGGAAGATGCAAATGTTCTCTGATGTCAC  
TGTCAAAAAAGAAGAACCAGTGGGTATATTGTATGCTTGAGTTCCAGCCA  
TTTGTCACAATAGATAGAGATGACTGCCATGTGTGTAGACTTTCTATAGA

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CTGTGTGCTAAACCCGA<sub>1</sub>CTGCCACTTCCAAGGAGTAGATGAGGAATG.C  
CATGGTTCTGGGGAGCCCTACCCCAATTTGGGGCAGACATTCCAAAGCTC  
ATTTTCTGTGGAGGGGGTTGATGGTTAAAGGACGGCCTGGGAGTAACTCG  
TCTGTACTAGGGCCCAGGAGAGTTACATGCTGCTTCCCATGTTATTTCATC  
ATTCCCCCATGTGAATAGCTATGGCGTGAGGTCCAAGGTTAGGGCCTTTC  
TACCATAAATGGGGGAATAAAATTCCCCTACCAGCCTGAGAAGTTTCTGT  
TATAAAGAGGCTTTTTTTTTTTCGGGGGTGGGGGAGCAAGCCGACTAATGT  
GTTATTTCCATACGGTTTGTTTTAAATGTAGATGTCATATGCAGGAGAG  
GTGGTGTAGTGAGTCACAACGGGATTAGAAGGACCAGTCCGAAAAGCAGA  
AGAGGGTCAAGTTCAGGGCACTGAGGACTACTGCATTCACTGGCGTGAAA  
GGCAGATGGCTGAACAGGAGGGGGACATTACATTGCTTGTTCCTTGAG  
CCTCGATTTCTCATCTAAAAAGAGGGTCATTTATTACAGAACATTTAT  
TAAACTGTGCGCAGGCACCGTGCCAGGAGCTGGACTAAAAATTAAATCCA  
CCCCTGTGAGCTGCTCTGAAGGCTAAAAATATGAAGTATGTAAAGTAACC  
AAGTGCTGTACACATGCAGCTATTCAATGACTGTGTGGGCATTGCGGCAG  
ATTTTAATTTTCTTTTTTATTCTTTCTCTTTAGTGAGAGGEGTTGGTTG  
TTATTATTGTCTGCTGTAACGTCTATTTCACTTGCTTTTTTGTGCTC  
TCCAGCCCATTCCAGGGCTGTCTAAGACACTTCTTATCACCTAAATA  
ACCGGGGAGGCAAAGCGCTTTCTTAAGAGATGGATCCAGAAGAACAATGC  
TGGTTTTCTGTAGAAAAAGGGGCTGTGGGAAGTAGAGATAAGAAGGGAAT  
TGGCCAAGATGAATGTACAGAGCCTTATTTTTTTTTTATAACACAGCAAG  
ATTAGATACAAAACAGGACAATAGCATCATCTGTTTTTATAACTGGAAAG  
GACCTCACTTTACAGGTGGGGAAGAATAGAGTGGAGAAGTGAAGAGAATG  
GTCACAGAGTCAATCAGCATGTCTGCGTCAAAGCTGGGATTCCCAATTCA  
GGGCTCTTACTACAGTGACGTATGGCTAATATTTTGGCATTGTTTCGGGG  
AAAAGCTGAAGCCCTGATGGTGTACGTCACTCTTGAGATAGTCTGTAGTC  
CAGCAGGGAGGAAAGCAAGGAAGGGAGGTGGAGGCAGCATTTTTTGGGTGT  
AACATTTCGTTCTTGTTTTGTGGCCAAATCATAGTGTGATTGGGACAAGC  
CACTGCCTTTCTCTGAGCCTCCACTTTCTTTTTTCTTCTTAAGAGGGAGGG  
AATAGTAGAGTAAAAGTAGTCATTTTATCAAACACCTGCTATTTTGGAGC  
CATATTGCAAGTGGGTGGGGGTGAACACTTGGCTTTATTACCCATAGG  
ATTAAATCCAACCTCGATACTGTGGCATTCCCAAACCTCCAGTCTAATCTT  
CTTCTCCATCAGCCATGCCCCACGACACCCTGGTCATATCTGATGTTGCC  
CCTTGCACTTGCCCCCTCCTTATCTTTGCTTTCTGACCTACCATATGGCT  
ATTGGTTGAAATTCTCATTTTCCAGGGCCTTGCTTAAATATCATCTCATC  
CATTAAACCTTTCTGAACTCCCTTGCCCTGCTTCCCTAATGTCTC  
AAGCCAGAATTTATTTCTTTTGTGGCCAAGGGACTGGGTTTGTGACCTC  
TCTCAGGAGACTTAATATTGAGACCAAACGTCTTTAGACCTCACCAGCCA  
GAGAGATGAGCATCTATGGAATGCAGGCTTTTGCCTGGACTTGCTGATGC  
AGGGCCTCTGCCTTCTCCAGGGCCTCTCTGCTGTTTTAGGAATTTCCC  
TCATGGCACAGTCCATGAGCTCAGGGTCAAGTTCATACATGTTTTTACTT  
CTTCTACTCTGCAAATGGTCTTCTTGAACCTCTGAGGGTCTAAAGCTGCT  
CTGCAGTTTGTGGGTGAGTAGAAAGGGGCTTTCAAAGTTGTGCTGTG  
TTTCCCACCCCAATAGCATGAAACACAAAGATGCTTACAAATAGCTGCCT  
TGCTTTCTAGTCCCAACTTCTCTCTCTGAGGCTTTAAAAACAAGTCCCCT  
AGGTTGAGCTGGACTGGAGTTGTATCCTATCTTCATTATCTGTCTACTCT  
CTTTCTGCTCTCTAGAGAAGATATTATATATGTGTGTATGTATGTGTAA  
TATATAATATCCATATATAGAACATATATTGTTATATTTACATATACATA  
CATAACATATGCATGTATTTCATATATACATATGTAGTATCAAAGTTGGAA  
TTAAACTGTATATTTTGTAAATTTGCTTTTATTGTCATCTATCACTGTAAA  
ATGAATATTTATCCATACCGTAAGATATTCTTCAATGTATTTTTTTTTT  
TTTGAAACAGGGTCTTGCTTTGTTGCCAGGCTGGAGTGCAATGACCCGA  
TCTTGGGTCACTGCAGCCTTGACCTCCCCGGCTCAAGTGATCTTCCCACC  
TTAGCCCTCTGAGTAGCTGGGACTAAAGGTGTGTGCCTCCACACCCAGCT  
TTTTAATTTTTTTGTATTTTTTTTTTAAAGACAGGGTTTTGCCACATTG  
CCCAAGCTGGTCTTGAGCTCCTGGGTCCAAGCAATCCTCCCCTTTGGCC  
TCCCAAGTGTGAAGATTACAAGCATGAGCCACCACACCTGGCCTCAATG  
TAATTTTTAATGGCTGTATAGTATTCCATCATGTGGTTGTACCCAAAATT  
ATTTAACCAGTCCCAGTTTATTTCAATTTTTTTTTTACTATTTTGAATAA  
TGTTTTAGTAAATACCCACAAAATATGTACAATGGCTGGGCTTAGTGGCT

FIG. 4 (38 of 61)

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CACCCCTGTAATCCCAA<sub>1</sub>ACTTTGGGAGTCTGAGGCAGGTGGGTCACTG  
AGGTGAGGAGTTCGAGACCATCTTGGTTAACATGGTGAAACCCCGTCTCT  
ACCAAAAATACAAAATTAGCCGGGTGTGGTGGCACACACCTGTAATCGC  
AGCTACTTGGGAGGCTGAAGTAGGAAAATCACTTGAACCTAGGAGGCGGA  
GGTTGCAGTGAGCCGAGATCACACTACTGTACTCCAGCATGGGCAACAGT  
GAGACTCCATCTCAAAAAAAAAAAAAAAAAAAAAAGTACAATTTGTTG  
TACCTCCCTGATTATTTCTTTTAAGTAGAATTTCTTATAATTTTTTTTA  
TAAGTAAAAATTTGAATCAAGGGAGAAGCACCTGGAGTCCTTCAGATACC  
TATTGCCAACTGAACTTTTCTGTTCCAGGTTTACTACATTCAGCCTGAC  
TCAGGGTTTGGGGAGTAGAGGAGGGGTGGAGGCAGAGGGCCTCTCCCTG  
TCCCCACAGACTCCCTTGGTGAGGTCCAAGTCTGGACAGGTGGAGTGTG  
GCATTGCACCGTCAGGTCCTGCTTCTGTAAATCCCCATAATCCATCCAG  
TGGAGCCTCATTGTTCAAGTCTTTTTTTTTTTTTTTTTTTTTTAACCTCC  
CTGAAGACGGAGTCTCACTCTGTGCCCCAGGCTGGAGTGCAGTGGCACGA  
TCTTGACTCATTTCAACCTCTGCCTCCCAGGTTCAAGTAATTCCTGCCC  
TCAGCCTCCTGAGTAGCTGGCACTACAGGCGTGTACCATCACGCCCGGCT  
AATTTTTTTTTGTATTTTTAGTAGAGACGGGTTTACCATGTTGGCCAG  
GCTGGTCTCGAACTCCTAACCTTGTGATCTACCCGCTCTGCCTCCCAA  
GTGCTGGGCTTACAGGTGTGAGCCACCAGGCTGGCCTCAAGTCTATTTT  
TTAACTCCAGGAGGCTGGTATTACAGAGGATTAGGGCTGGCAGAAGGGC  
CTCAAAGCTTTCAAGGCTGGGGAATAGGCTGCAGCCTGGTTCAAGGTAA  
CCCAAGTGATTTTGGTTCCAAAGGGACAGGAAAAAAGTGATTGATATGG  
AAGTTGTCAAAGTGCAACTGTCAAGACATTAAAAATGTAACCTTTTAC  
TAATATACAGTAGACTTGTGTTAAATATTTAACTGATTGTAAAGGAAAA  
AACAGACGCAGTTTTCCCTACCACTGTCAACACCTCAACACTGAG  
TTCTTCTGTGACCTCTAGTCACCGAAATGCTTGGGGATTTCTCCACCAC  
TAGTCTCCAGCAGCCGACACCAGTTGGGTGTCTTAATCACTCCAACAC  
TATCTACCTGGAGTTAGCGTTAGATCCACAGGTTGAGGGCTCAGTCTCA  
CAAGACTGCCTCCCACTTCAGGTGCCAGTTACAAGTGGTAGGTTGTCACC  
TATGCTTCTGACTGATGGCTATAAATCTGGGTTTGCTTCCCTCGGGTTCC  
GTGAATTTGCTAGAGCAGCTCACAGAACTCAGGAAAACACTTAAGTTTAC  
CAGTTTATTCTAAAAGATATTACAAAGGATACAGATGAACACCAGATGAA  
GAGATGCGCAGAGCAAAGCATGTGAGAAGGGGTGTGGAGCTTCCATGCCC  
CTCTGGGGCACCACCTCCAGGAACCTTCATGTGTCCAGCTATCTGGGAG  
CCCTTCCAAACCTGTCTTTTGGGTTTTTAAGAGTGGCTTTATTACAT  
ACACATGATTGACCGAACCATTGGCCATTGGTGAAGTACACAACCTTCAG  
CCCCTCCACTCCCTCCAGTGGTTGGGGAGTGGGGCTAACAGTCTCAAGTC  
TCCAATCCTGCCTTGGTCTTTCCTGTGACAAACCCATCATGAAGCTACT  
GCATTGGGGCTGCCAGCCAGTCATCTATTAGCATGCAAAAGACACTC  
TTATTATTCCAGAGATTCCAAGGGTTTTTAAAGCTGTATGTGAGGAAAC  
AGGAGATGAAGAACAAATATATATTTCAACATCACACTCGTTGGGGGA  
ATTGACAGGATAGCAAACTGATTAAAGGAGGATAGGAGAGACTGAGATA  
TATATTTCCATATATATATATAGAGAGAGAGAGATATTTCCATATATA  
TATATAGATCTAGAGAGAGAGAGATAGAGAGAGAAGAGTCTTTCC

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ACACATTTGGGGGAGCAGTTCCGGAGGTACAGCCCGGACAGGAGATGTGA  
GAAGATCGTGGTTANTGTTCCCTGGTCCAGAACCCTCCAAGTGGGCTT  
AAGTAGGAAGGGTGGTGAGCGGCAGGTAAACACACGTCAAAGGCAGTCTT  
CCTCTCTGAGGGAAAACACTTGTATAAGCATTGCAATCAATGGGCCTCTT  
TAATTATGTGCCAGTGGCAAGAGCGGGTGCTGAACCCAGGGGCCTGCCTC  
AATCCGGGGCCTTTGAGGCAGAATAAAGTGGTCTCAGGTTGTTGGCATT  
CCTTGCCCTTCCACCCGAAGCAGACACAAATCCTCTCTGGAGGCAAGTTC  
CCCAATTGAGCCAGTACAACCTCCACAGACTAAGATCAATCATGTACAAG  
CTCACAGACAAAGGTCAACCAACACACAGAGCAATAAACAAATTCATGAG  
TGACGTGAATGAGAATAAACAGAAACAATAACCACCAGCTGGGATGCTCT  
AAGTCTTCAGCTGTTAGAATTCCTGAATATAGAATAAACTGCCACAATG  
GCAACATGCATCTAGTACTTACTGTGTGCTGGGTTCTAAGAAATTTGCA  
CATTGTGCCAGATACCGACTCAGCTTCACACTCACCTCCTACTGTGCC  
TCTTAATTTGCACTAGATTAAGGTTAGAAAGGAAGAGGCAGCTATTCTG  
TTCTTGGCTGTGCTCTGGCAGCACATGCAAAATGGGCAGTAACAGTGGC

AGTCACAGGTAAGTAGT TTCTCACAGT JGGAGTTAAAGGCATGGGA  
GAGACGAGCAAGGTTCTTAAAGGGACAGTGGCCAGTAAATGACCAGGGGC  
TACTGGAGTGGCTGCATGGCTCTGTGGAAGCTCAGAGGAGCCTTGGGTCC  
TGCAGGTGCAGTAGCAGCTTTCTGTAGTTCTGTATCTCTGGGTCCCACAA  
TCTTCCCCGTTTTTGCTCCTCCACTTCTAATTTTGTAACTGACTTCCCTG  
TGTGTACTTCTCTCTCTGATTGAAATAGCCAGACTGGTTTCTGTTTCCTG  
ATAAGACATTGTCTGGTACGAACACAGTAACCTATTTAATCCGATATCTC  
TATGAAGGAGGTACAATAATTATTCCTATTTTACAGATGAGGAAACACAG  
CAGAAAAATAAAGTCAATTGTCTAAGGTTGCACATTTAGTCAAGGGAAGG  
GTTGATATAACATATAATTATTTAGAAAACATCTAAGGAAATAAAAGGCA  
TAATTTAAAAATAAACTAGGCAGGTTTAAAAAATGAAGTAATCTATAA  
GTAAAAAAGTATAATTGTTGAAATACATATCTTAGTGGATGGGTAAATA  
GCTGAAGAATGATTAATGAACCTGGAAGGTAGTTCTGAGGAAATCAGAAT  
TCAGCATAGATAGAAAAAATGGGAATTTACAAAAGTACACAGGAATTATA  
AAAGAGGTTAAATTATAGGGAGGGTAGAATGAGAATTAACATTGGTCTAA  
CTGGAATTTTGGAAGAAGAGAATAGAGAGAATGAACAAGGCAATATTTAA  
AGAGGTGGCTGAGAAATTTTTCAGAACCAACACAACTATGACTTTACCAG  
TAGAGAAAACAATGTACACTGAGGAGGATAAATAAATACTATGAACAA  
ATTGTAATAATAACTCAACAAAGACAAAGAGAAGATCTTAAATCAGC  
AAAAAAGAAAGTCAGACTTAGAAAGAAATGACAATGGCAGACTACTCAA  
CAACAACATGGAACCAAAATTCAGTGAAACAGTATTTCAAATGCATA  
TTTAATCTATCTTTGAAGAATAAGGGTGAAAAGGGTGAAAATTGCTGCCT  
TATACAAAATATCAACATTAACAAAAAGTAATGAAGTAATATAAAAAATG  
TTTTCAAATAAACAAAAGTGAAGAGTTTACCACCAACAAGCATTCTTA  
AATGGACTTTTAAATGCAGTTTTTAGGAAGAAGGAAAACAATTCCTAAGG  
AAGGTCTGAGATGCAAAAAGGAATTATGAACAAAGAAATTGTTAAATTA  
TAGGTGAATTAAAAAAGTGCCTGCATAAATGATAAATGACAATGATG  
CTATTAATAATGAGTTGATAAGGATAAAGAAAAGGACAGAATTAATAAC  
TAGAAAAACAAGCTGTGGAAGGATTCAGGAATTACTTGAAGGTTAAAG  
TTCTAGGGTCTCTCTATCCTTCTAGAGGGGAGTCAATATATTAATTTTTG  
ACCGTCACTTACACAGTGAAAACTTTAAGGATAACCAATAAAAAATAGA  
AATAGAGAGTATAACTTCTGAAACAGTCAAGGGAAAAATATGGAATAAGA  
AAACTGACCAAAAAACATCTCAGTCAATCAAAAAAAGAAAAAGAAA  
GAAAAGGTTCTGGAAGGAGAAAATCAAAGCATAGAAAAAGCGGGACAAATA  
GAAGTGGAAAAGAAAAGGTAGAAGAAAACAGGTCCAGAAATATCACTGAT  
GCACTAAATCACCATTAAAGATGAAAAACAAATGAACAACATCAAAAAAT  
TCTAGTGACTGTAGTAGTGCTGATCAGAATAGGCTCTAAGATAAGATGCA  
TTATTGTGAGTCAACTTGTGATGATGAAAGGTTTAATTCACCAGAAAGAC  
ACAATTATAAAGTTGTAATCAAATAGTTTTATTTTATTTACTTTATTTAT  
TTATTTTTTTTGGAGACAGGATCTTGTCTGTTGCTCAGGCTGGAGTGCG  
TGGCTTGATCTCAGCTCACTGCAGCCTCCACCTCTTGAGGCTCAAGCTTT  
CTTCTGCTTACGCTCATGAGTAGCTGGGTCCACAGGCACACACCACCA  
AGCCCTGCTAATTTTTGTATTTTTGTAGAGATGGGGTTTTACCATGTTA  
CCAGGCTGGTCTCAAACCTCTGGGCTCAAGCGATCTGCCCCCTCGGCTT  
CCCAAAGTGTGGGATTATAGGCGTGAGCCACGGTGCCTGGCCTCAAATA  
ACTATTTAAGTGAACAAAAGTATGATGGCCTAATGAAAAATGTATAAA  
TCCATAATCGCAGAGGGATTCAACTTACTTCTTTGATTATGTAAAGGT  
CAAACAGACAAAAGACAATGACAAAATTAATGCAATGAACACTTTTGAT  
TTAATGAACATATATTGGATATGTACCAAGAATTAGAGAATACATACTA  
GTTTTGAGTTTATGCAGAACATTTACAAAAATTTAGTGGAAGCCTAAAT  
ATAAAAAGTTGCTGTACGTAGAATAACACACAAACCCCTGAGTCCGGAA  
TTCAAAGCCCTCCACACTCTCCTCTACCTTTGCATCTTTATCCTCCACCA  
CACTGCAGTGCACTCTGGGCTACTACTCACTGTTCTTGATTCAAATTC  
CATGTTCTGTGAGCTCAAATCATTCTCTCTGCTGGAATAACTACTTCAT  
ACATATTCTGCTATTGAATCTTGTCTTAGCACCCCATCTACTCCAAGAC  
GATGTCAGTTGGGGTTACTCCCTGTCCATTTTCTTTGATTACACTTTT  
TTTTTCTACTTCCATTATATTATGATCACATCTGTGCCACAGTTTGTGA  
CTTTGTGTCTGCTTTTACTCTTTTCTAGACCCTGAGAGCTCCTGAAGGT  
TGGGTCAATTTCTTTTTTATTGCTCATTCTCATGGCACAGTGAGTGCTT  
AATAAATGGCTATTGACTGAAATTAACCTGTATCTAAATGGACATATTCC

FIG. 4 (40 f 61)

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ACTTCTGGGCCATTCACTTTCTTTCTATTGGAACCAGGAGATGGGGAA  
CCATAACAAAGGTAAGGTTGTGCCATGTGAAAGAACATGGAACCTTCCCC  
TGAGGGCCAAAAAGAGCAGGGAAAGGTGCAAAGACAAAATCTTCCATTT  
TTAAACAATGTAAGAATGTGGTCCACCTCATGCTCAGGTGGGACTTTATC  
ATGACGTTATTTTTGGGGACTTATAGCTGCATCATTTACCCCATATACAT  
TTACCTTTAGTGTAGGGAACTGAGGACAGGAATTTTGTGATGCAGACTC  
TTGCTAATGAGGCTAACACTTTGGAGAATTTTATCATGCATTCAAGAAGC  
TTGTTTTACATTTCTTCATTAATACTTTAGTTGGTGGTTTAGCTTTAGTT  
GTAGGCTTATCAGATATTTGGAGATATCTTCATAAACGATGGCTTTGGTT  
TTAGAAGGTTATTCTGAAGCTACTATTTCTGGCAATAATCAAACAGCAT  
GGCCATTTGTTTTGTAAGGCCTTTCTTAAATATGACGGTAAATCTACG  
TGTGGAAAAATGCTTATTCTTCTGTCTCTATAAATGTGAATCTAGTTTG  
TCTTCAAATGAAATCAAGTGATTAAATGTAGTTTTCTAAGAAGATAAA  
TGGAGCAAAGCACTCTGTGTTTACAGTGTTGGAAATCACTCATCCCTCA  
TAAACTGTCCCACTGATCCTGACTCACATGAATGAATTAATAAGAG  
TTAATAACATCAATTTACATTTTAAAGACACTTTCCCATGTTTAGACT  
ATTGGTTGGAAAGCTGGTAGGTGTACAATTTGTGGAGAGTTGGCTGTTT  
TTGTCTGTGTTGTTGACGTATTTCAAAGCCATATCTAATTTTGTGCA  
GAATGGTCTGAATTTACAAAAATGTTGAGTTGTGTAGTGTGGAGAAGTA  
CGGAGCCATTTACTGAAAGGCTGGGGGGAAATGACGAGACCCTGAGATAA  
GGCAGTAGTGGTGCGAACAGAGTGGAAGGGAGGTAGTTGAGATATGTTCA  
GAGTAGAATCAGAATGGACATAGTGAACCACTGGATGCAGGTGGGGGCTG  
AGGAAGCAAAGTTGAGGATAATTCTGAGACTTCTAGGTTGATCCACTGAA  
GTTACATTATTCAACACCACAAGGAACTAGGGGAATGAGAAGGCATACT  
GGTTTGCTTTGGAGTGAAGGCGAGTGATGTAAGAGGAGTTAATGAGTTA  
AAGTTTGATATGCCTGAACCTCAATTTGATATGTGCATCTGATATACCC  
TTGGGGTGACCCTCCAGGCAATGGTTGAACATGTGTATTTCTTAGTAAC  
GATAGGCATCACAGACTCACATCAGTAAGGAAGCAACAGCAAACCTTGATT  
GGACGATATACCTGGAACCTCAGTACCCTATGACTGGAGCAAGTCTCTGTC  
AGTGAAATGAGGATAAGAAGATCTTGACCTTGTGGAATATGTTGTTAGG  
AATATATGTGATGAACAACATAGGATACTTCTACAGGGCTCCACATGTA  
GTAAGGGCTTTATAAATGCTTGATAAATATTATTGTTGTAATTTATTTC  
AAAGTAAGATGCCACTGGAGGAATCTTTGGAACCCAAATTAATAACAAAT  
AGGACTGGATGCAATGGCTCACACCTGTAATCCAGCACTTTGGAAGGCC  
AAGGCAGGAGGATCTCTTGAGCCAGAAATCAAGACCAGCCTGGGTGAC  
ACAGGGAGACCTTGATCTATGAAGAATTAATAAATAAACCAGATGTG  
GTGGTGACGCTATAGTCCCTGCTGCTTGAGAGGCTGAGGTGGGAGGAT  
TGCTTGAGCCCATGAGGTTGAGGCTGCAGTGAGCCATAATTGTGCCACCA  
CACTCCAGACTGGGTGACAGAGTGAGACCCTATCTCAAATAAATAAATAA  
ATAAATAAATAAATAAGTACAAACCAGCAAACACTAATCCTTTCTAGAGA  
TTATTGAACTCTGGAGGGCAGATCTGAATGGAGCCAGCAGAGGGACCTAT  
GGAGATCAGCCTGGCCCTGGACAGCACCAGGCAATGGGGTTGCTAGAGAG  
GTAATGGGGTTGAACAGGGTTTAAGCCATGAGGTCTCAAGAATCCGTGAA  
GACTCAGACTAATTTTTTTTTTTTGCATGAGGATTAGGTGTTCTTAGGA  
ATTTCAATGAGAGCAGGGTTAATGAAGGAATGCAGGCTAGGAGAGCTGAG  
GGAAGGCATCTGAGAGAGCCTGGCTTATGAATGGCTGCGTCAGTATGGCT  
CACCTGCTTTCTTGTATCTACTTAGCAGATGATCCCACCCAGGCCTCC  
AGGGCCAAGGTCATTTCCACATAGTCATGGGCCCTTGAGGGCCTGGAGCA  
GTGTAAGGAAGACAGAGTCTTAAGAAATTGCATTAACAGTCATGGTGCTT  
GGCAAGTGTGCTCATCTATGCCAAGCCTGATCTGAAGGGGTGCATGCTC  
ATAGGTAGCTGCTGCCAAGATTACAGCAGCTTCTTCAATCCAGATCCA  
TGCTCTCCTATATTCAATTTTCCAGGGGTTCTGTCTTTCGACAGTGATG  
AGATGCAATGACTTATTGAGTTATTCTCTGATAGTTGCCAATTTTTC  
CAAATGACAATGGGGCATGGAGCTTGAGAGTGGAATGAGGCCCTAGGGA  
TAGCGTGCTTAGGAAAACACTCCAGCCTGATGTAATCTGGGGGTACAA  
TGGCATTTCATCATCAAGACTGATGTAAAGGGTGACTAGCAGTGAGTTG  
GGGGTGACTCGCACTGGGGCTAGGTTTCTGATTCTGCCTAATCCAGACAG  
AGCAGAAGCACTAGTGGGCTGGTAGAGGGCCTCCAGGGCCTCACTTAATG  
TCCTGGAAAAACAGCTCCAGATTGTTGGTTTACGTTCTGAGGACAAGCTT  
GGGTACTACAGGATAGAGAGAGTGGTGGGAGATGCCGTGGCCTGCCCTGC

FIG. 4 (41 of 61)

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TGATGCCTGCCCTGCCATTCTCGCGTGTGATGTCTCTGGGGCATCTTGCC  
TTCCCTGCCAGACCTGTAGTTTCTGAGGGCATGTGGAGGCCAAATGG  
CTTCTTAGAGTGTACTTTCTTGAACAGCTCTGCTGGGAGAACTGGAGG  
AGCTAGCTAGTCACGGTAACTGCAGCAGTCAAAGGATCGTCCCGGTGGAG  
GTGGGGTGGAAAGGTAGAGAAAGAGAACATATAGCGTTTTCTTGAGAT  
GTGTGGGCATGTATAGAGGAAATACCCAATTCCTGAGCCTTGAGCCCTC  
CAGGAAACCTTGAATATTAGGTAGTCATCCCCAAGGAAGTCTAAGAAT  
TCTGGTCTCACCCTCTCCTTTAATCCCACAATGATCCTACATGATATT  
AAGGAACACGGGCCAGTAACCCCTCCAAGCAATGGATGTGGTGGTGAAGTT  
TGACCTCATGATGGAGCGGAGGTGGTTTTGAAACCTAAGAATTTAATTTA  
TTGTTTTCAAACCTGTTCTCAGCTCAGCGTTATTAAAGCATAACATAATTGAC  
ACATAAAAATTGTATATGTCTACGGTGTACAATGTGATGTTTCGATCTAT  
GTATACATTGTGAAATGATTACAACAAGCTAAATAACATACCCATTTCATC  
GTGTTTTCAAAGGAATTAAGTCAAGCACAAAAGAGAGGTGCTGTTGAAGA  
GTAGGGCTGCTCTATCTAAGTAGTATGTCTGGGGTGTCTGGATCAGGG  
TCCTTTTGTGTAGTAATAAACAGCCCTTCTGGGGCTGCTCAGCTTTCC  
CCACATTTTCTTCTGGAGCCTCCCTAAGAATTAGGACATGGCCACTTTCT  
CTGCATAGGCTTCTACTTCAACAAGGACAGGGCTTGTGCTGCCCCATGC  
CACTTGAGTGTCCCTACAGCACAGAGCTGAGTGCACACTGGCTGAGTGAG  
GAAATCCCCCAGATTATCTTGGTCTAAGCATCATGGCTGTATTTCA  
CGTATATGAATTACAAATTACAGCATAGTCGAATAAGGATTTTTGTGCTA  
CAACTGGAATCCCAGATTATGCAAATTGGATAGTATAATATTGAAATTC  
TAGGACTTTTTATTAGTTTTAAAAAATTATACAAGCTTAGAGTAAGAAAT  
TAAACAGTGCAAAAGAAATTCAGTGTGAAAAGTAAATGCTGTCTCTGC  
TGAGAGACAGATATTGCAGCCAGATACTACTGGGGTCAATAGTTTTCTT  
TAAGCATGCCATTTTGATGGTTTTATGGGACTTACAGCTCAAGAAGCTTGA  
CACTAGGGTTGATCTCAGAAAATCATTGTTGCAGGTATTAGATATGACCG  
TCTCATAAAGATACACACACAGACACAGCGATTGGAGATATTCAGTGGG  
CTTATGGGCTGCTTGTCTTTCTGCTCTGTGCCTAAGTTGGGCTCAGAGT  
AGCCTGGCATCGGCTGTGGGAGAAATGCTGGCATGGGGTTAGCAGGAGCC  
CACTTAACATGTCTTAAGCCACCTGGAAGAGTCTTCAAGGAGACCAGAC  
TCCAGAGGCCCTAAGGAAGGAAGGACTTTTGCCCGTTTTTAGGTATTCTA  
GTCCCAGAGTTTAGGGAGGAATGGTTTTGGCTTTGGGTGCTGTGCCCCTTT  
ACCGAGTGGGATGGGATGTGCCCATGAGCTGTTGAGCTGGCTCTTGAGGA  
AGACAGCAAAAGCGGGAATAAGAGGTCAAGGAAGCTGTGTGGTTGTAGGAA  
ATCCCAGCAGAGGGCTGGGGGTCAAAAGTGGTCTAGGTAGTGACGGTGG  
AGGCTGAGGTGGTAGAAAATCAGAGGACAAACCCCATGGGCTGCTGGTGA  
TCTGACCGAGCTCCTATGCTCTCCTGGTTCATTTTAGGCTCTGTAGCAGC  
AGATGATTGGCTGGTGTGAGAGCAGTGCACCTGCCATATCAGGCAATCCA  
AGACAAGTCCAAGCTACGCTGGGAGGAAACCTGAAGGCAGCAGCAGGTAG  
ACTGGCTGAAGACAGACAGGCAGGCAACTTGTCAATCAGATTTGTGTTTT  
TAAGGACTTTTAACTGGGGAGCCCTCCATGACAGATCAGATGAGAGAGGA  
ATCTGGGTCCGCCCATGTGTCAAGCTACCAGAGGGTCCCATCGGTGCTTG  
GATCTTCTTTGAAGCTGGGTCTGAGGTTTTGCAGGTAGAGGGTGAAGTGGT  
CAGAGGACCTATTGCAGAGCTAACCAACACCTTCCAGGAATGCAAGCA  
CAAGCACCCACCGCGGGCAGGCGGGCAGGCACTTCTCCTTTTGCCACCA  
GGACCTCACAGAGGCTGATCTGGCTCTGTGAGGTGGGAAAATGGGTGTGTA  
CTTAGTACATAGAGATAAAAGGCTTAGGAGGCCCCCTCCATCCTGTGACCC  
TGTCCCCAGACCACAGGTGCCCGCAGGTGCTGCTATTTCAAGGCTGGGCC  
TCAGTGCAAGCTTGTGGTTTTCTTGCCACCTGTGATGTCTCCCACTAAT  
GAAGGGGCTCTCCATCCTCTGTCTGCCTCTAGCAAGTGGAGGCTCTGGGC  
CCTGGGCAAGACACAGGGGGAAATGCCATCTGTTATCCAAATATATTTCA  
ATGTGACAGGAAAGCTGTCTTTAGAGCACAGC

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GCATGTGCTCTACATTGATCCCAGGAGTTTGAGACAAACATTGCAAGACTG  
GGCAACAAGCAAGACTCTGTCTCTACAAAAAATAAAAAAATTAGTTGGG  
CATGGTGGTACATGCCTGTGGTCCCAGCTACTCCTAAGTTGAAGAGGGAG  
AATTGCTTGAAGCTGAGGTTCAAGGCTGCAGTGAGCTATGATCACACCA  
CTGCACCTTANCTGGGTGACAGAGCAAGACCCTGTCTCTAAAATAATAA  
TCGTAATACATTTTTTTTAAAGTAAACAAAAAAGGTCACACTTTCTCA

FIG. 4 (42 of 61)

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TACCAAAATAAATTCCAAATAAATTAAAGGCTTAAACATGAGAAAGTTAA  
ACCATAAAATTACTAGAAGAAAATAAAAGCAAATATTTAGATAATCCTGG  
GGATAAAATTTCTTTGGAATGAATTTCTTTAAGATGAATCTCTAAAAGTGA  
AATTCAGGGTTCAAAGGTCTTTTCTTTGTCCTTTTCTTTTCCCTTTCCCT  
CTCCCTTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCT  
TTCTTTCTTTTATCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCT  
TGTTTGCTTGCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCT  
TTCTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTT  
CTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTT  
TTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCT  
TCTTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCT  
TCTTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCT  
AACAGTCGCATGAACATGGCTCACAGCAGCCTTGACCTCCTGGGTTCAAG  
CAATTCTCCTGCCTCAGTCTCTCAAGTAGCTGAGACCAAGGCACCCACC  
ACCAAACCTGGCTAATTTTGTATTTTGTAGTAGAGATGGGGTTTACCAC  
ATTGGCCAGGCTGGTCTTGAACCTCCTGACCTCAGGTGATCTGCCTGCCTT  
GGCCTTCTGAAGTGCTGGGATTACAGGCTGGGCCTCTACGCCGGGCGGAG  
ACTACCTCTCTTTTAACTGGATCTCTGAGCTCTGGGCAGAGCCCACCTG  
AATCCTGGTCTCCAAAAGGGAAAATTATTAGGAGGCTAGACCATATGAT  
GCTTTTACAGTGCACTTAAAAAAAGTTTGTTTTTTTTTTAAAAAGACATT  
TCTACATGTCTAACTACAATCTTCTTTGAAAACCCAAGAGTAGCTTCTG  
TTGCAATAGCTAGTCAAAAATATAATAGTCAAAAAAATCAGGTAAACACAA  
CACAAACGCAAGCAGTTTAAAGAGCTGAAATGAACTTGTCTGTTTACACTC  
TAGGGATTCCATAAGGAAAAATAGAAGTTTCTCCCTAAAAGGGAGCCTGG  
CACCTTCTCCATTTTCTTTAAGGAACCCAGGCTATTATAAACTATTTTA  
GGGCTCTCATGCAGCAGACGGTGCAAGAGAAAGGAGAGACAGCAGAAGTA  
AATGAAGAAAAACAGAATCCAGTCAACAGAGAAGAAAAAACTTTTGCTCA  
AAAAAAGGCAAGTTCTTAGGAAAGAAAAAAACATGAGGGCTATTTAA  
ATACAAAGACGCATACATACACATGCACACATCTTGGATGTAGCTTTTA  
ATTAAGCTGACTTTTAACTATTGAGGTCTTTAAAAATAAATCTTTTAAAA  
TCTTATTACGATATTTTCACTAGGACAAATTGCTGCTATTTTCAACATTAC  
CAAGTATCAAACCAAGAAAGGCTTGATTTAGGAACCAAAACCCAGGCTGTC  
GTGGTAGGAAAAAAGGCAGAACGTTAGCTATGGAACCCACAGCATGGGGC  
AACAGCCATTGCTCTTTCAGTATGGCCTGGCTAGCAAAAAGGTGGCCTTG  
TTATGTAAATAAAGCCCGTTTGGTGGTCAAAATGAAACATCTTTTCTTTT  
TTTTTTCTTTTGTCTGGCCGTTTTTTCCCCCACCATACCAGTTTGTGT  
GTGTGGGAGGGTGGGAATTTAGCCACTTCAGAGGCCTCATTTCCCATAAAT  
TTGGAATTTCTTTTGGATTTGATCAAGTCAGATAGAGTAGGTCAAACCC  
AATGGGAAAAAGACTGAAACAGCAATAAAAAACAGAAACAAACAGTTAAGC  
AAAATGAATGATCACACAACCTTATATGATTACTGAGTGCTCTAATGGTAA  
GGAGAAATTAAGACCAGCTGGTTGTTAACTTTAGCCAAGACAAAACCCC  
AATTCAGCTACTTACCTAGGGTTGGGTCTCAGGCTGAAGACCGCTCACTA  
CGTTTCTAGAAGCAAGAAATAAACTTGAACCTCGTCTTACCTGTGTAGCA  
GGACAAGCCGCAGACAAAATCCCTCAGACACCAAATTAAGAAGGAAGGG  
CTTTATTGGGCCTGGAGCTGCGGCAAGACTCACGTCTCCAACAACCGAGC  
TCCCCGAGTGTGCAATTCCTGTCCCTTTTAAGGGCTCACAACCTCTAAGGC  
GGTCCACATGAGAGAGTCGTGATAGATTGAGCAAGCAGGGGGTATGTGAC  
TGGGGGCTGCATGCACCTGTAGTTAGAAATGGAACAGAACATGACAGGGAT  
CTTCACAGTGCTTTTCTTATGCAAATAACCGATTAGATCAGGGGTCGATC  
TTTACCAGGCCCAGGGTGTGTACCGGGCTGTCTGCTTGTGGATTTTATT  
TCTGCCTTTTAGTTATTACTTCTTTCTTTGGAGGCAGAAATTGGGCATAA  
GACAATATGAGGGGTGGTCTCCTCTCTTACCTGCGGGGAGTGAGCTCAA  
CTCCTTAAAGGAGTTACCTGCCTTCCATCATCAGGGAAGCAGGAAATCTT  
GCCTTCTTGTGGAAGCAAGTAAACTCAAAACAAACAAAGAAAAAAAC  
AGGGAGTTGTACAGCAAAATAAATTTTGAATTTTGACCAAATTTTGGGAG  
ATCAGGAATCTCTGAAGGAGATGCTTTTCAACCTCAGCAAATTTGTCTGT  
TTGGTTTGAGCCATAAAGTTAGCTCATGCTGGTACCAACACCAGTAGGA  
GATTTGTCAAAGGTAAGAGGCATCTCCACTCAGAATCCCTTCGTGGTTAC  
CAACATGTGAACCTTGGAAATCTGAGACAGGTCTCAGTTAATTTAGAAAG  
TTTATTTTGCACGGTTGAGGACACCCACCCATGACAGAGCATCAGGAGG  
TCCTGACCACATGTGCTCAGGGTGGTCTGAGCACAGCTTGGTTTTACACA

FIG. 4 (43 f 61)

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TTT TAGGGAGACATGAGACATCAGTGAATATATGTAAGATGTACACTGGT  
TCCCTCCAGAAAGGCAGAACAACTTGAAGCAGGGAGGGAGCTTCCAGGTC  
ACAGGTAGGTGAGAGACAAACAATTGCATTCTTCTGAGTGTCTGATTAGC  
CTTTCCAAAGGAGGCAATCAGATATGCATTTATCACAGTGAGCAGAGGGG  
TGACTTTGAATAGAATGGGAGGCAGGTTTGGCCCTAAGCAGTTCCAGCTT  
GACTTTTCCCTTTAGCTTAGTGATTGGAGGGCCCAAGATTTATTTTCCT  
TCTACATCACTGTGGGCAGCTGACTAGGAAAGCTTTGTAGGACTGGTGGG  
CAGTGTGAGAGCCCAGTGGGGGGTGGTGGTCTGTGCCAATGGTAGCAAC  
CACCTGTGAGGCTGAGTAAACTCATTTCCTCAACCTCCTCTAGCAGCCCCA  
GTGGAGATACAGATGAAGCAGACTAGCGATACAACCCAGCCTGAAGTTTT  
GTCTGGTGAAGTGAATGGAATAAAAAATGGGAAGGGTGCTGAAGAGACCAG  
CAAGAAAATGGTTGAGAGATGGGGCACAGAAATTAAGCTGGATCAAAAA  
GGACGGAAAAGCAGAAAGGGCCGATAGAGAGAGGGGATATCTATGGGTTC  
GCGATTCTGAAAAGGACAAATCACTGGTGCTTTGAGAAGAGAGAGGGTGA  
GAAAGCAGGAAGGCTGGAGGCTGTCAATCAAGAGGGCGACATCTGTGAAC  
ATGATTCCAAGTCACTCAGACCATGGGGGTGGCCAAAGGAGTGCCCTCT  
TCTCACCTCCTACTCTTAATTCCTTGACTCAAGATAATAAGTTCCCAGA  
AGAGAAGTACCCATATTTAATTCATCTGTGTCTTCTAGCAGTACTAAAA  
ATATTATATGAAAGGTATCAAACTTTGAGAATGTGTGCTGTAAATTGT  
TAAGGATGCTGGAAAACCTCAAGACGTCCCTGATCCTGAGCCTGAGTATGA  
GCCTGTGGTGAGCCCAATGCAGGTCTCCATTGAGACAAAGGCCTCAGGGA  
ACGGATGAGACCTAGGGACAGAGATGCATGCTGGAGCAGCATTCCCCATC  
CCTACTGCAGCTCAGGCCAGCTGACTGCTTTATGAGTAAACGTTACCAGG  
GAACACTTTGCAGTCTTAACACACATGCCACCTGTGACCACTGATCCCT  
GTTGGGTGACCACTGACATCAGAGATTGATGGCAGCAATGAAGACAAGG  
CTATCCTCATTAGGAAGGAAAGGAAGGAGGAGGGAGGGCAAACGAAT  
CTTTCCTGCTTGTCAACCACGTCCATCTCTGTAGGTGATTTCCCATGTG  
TGACTTTGTTTATCTTTATAATAACTCTGAGAGGTAGGTCTTGATGTCCA  
CATTTTGAACATGAGGACATCCAGCCAGGAAGTTGAGTTCTGGGGACATA  
GCTGAGAGGGCAAAGCTACATATAAAACCCCTCTTTGTTTTTTCTGGCTTA  
TCCACTGAGTGCCCCCTGCAATCCACCAGCCCATTTGTGAAGTGCATACT  
ATAGGTAAGTTGGCACAGGAGGAGTGGATGTGGGCGATTTTGTACAGCT  
CTCCAGGAACTTACACACTGGTGAGGAGGGCCAGGTATGTTCTTGACCAG  
TCACAATCAAAGCAACCTCCTACTAATCAGGGAGGCTTGGTACCTGGGGA  
ATGCTATGTTGAAAGGTTCTTTCTGGGTTTTAAATGATGGGTCTATTT  
CCTTATTCTTAAGATTGCTTTTCTGGCTAGAACTTAAAGAAAATTTT  
CAGTAAATTTCCCTTCCCTGGCACAAAGTGAGCTTGAAATGAATTCCCA  
GGTGGCCTTGATACTTTAAATATTTGCCTCCTATAAAATCAACCTTTAGA  
AGAAGGAAGTCAAAGAACATGCTAGATTTCAAAGGTTAATTCCTTGAA  
ATCCAGTTATCTACAGGACAATGTTGTCAAAGAAAAAATTATTTGGCCAG  
GCACGGCGGCTCATGCCTATAATCCAGCACTTTGGGAGGCTGAGGCAGG  
TGGATCACCTGAGGTGAGGAGTTCGAGACCAGCCTGGCCAACATGGTGAA  
ACCCCATCTCTACTAAAAATACAAAAAAATTAGCCAGGTGTGGTGGTGG  
GCACCTGTAATCCAGCTACACGGGAGGCTGAGGCAGGAGAATCGCTTGA  
ACCCGGGAGGAGGAAGTTGCAGTGAGCCAAGTTCAAGCCACTGCACCCCA  
GCCTGGGCAACAGAGCAAGACTTTGTCTCAAAAAAAAAAAAAATTCAT  
GATATTTTTAAATTCATGGTAAGGAAGATTTCAATCAGAACCAGCACAGA  
AGATATAGGAAACACTGCAATGGGACTTTGCGGTGGGGGAGAGAGATTGA  
ACACAACATACATATACAGCACGGGCAAGGACATATTCATAGCCAGGAAGC  
AGAGCAAAGATCAGTGGATGCGAAATTACTAAGAGGAAACATGAAAAATA  
AGGGAGCTTCTGCCTAAACCCACCTAACCAGATCCTTGCTGAAGACAGGA  
CAGGGTGATTGGACACCACTTTGGGGATGGTGGAGGATGGGGAATCCAGT  
GAGATTTCAAGGGTGATCAGATATTGAACATAGAAGGTTCTTGCTAAAAA  
AGGAGTTTACAAGAAAGTGTAACAATGTGCCTGGGAGAAGGTTCAAGAGC  
CTGACTAAAAATTTGGTCAAGCAGAGAATATTTGCCAAGATAATAGCTAAG  
TCTTCTGACAAACAATAGATGCTAAGCCAGCAAGGGTGATGTGCTCAGAG  
AAAGCACTGAGGGCTTATTTCTTTTCCCCCAATCTCCACTCAGTCAAGT  
CTAGTCCCTTGTCAATGTAGCCATTTGTAAAGATGCAATCAGGCAGGGT  
CCCATCTCCTAGTGACAGGACTGACTGAAGTTCTGCTGAAGAGAGTGGCC  
TGGGGCTSACACCGAGATTTCAGAGTCTGGGTTTGGCCGAGAGCTCAGT

FIG. 4 (44 of 61)

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GTAGTGCCATGCCCTCTCTCCACCTGAACGCCAGTGTGGGCAGGAACAA  
CTGCAGCTAGAAGTCTGGCACTTACGCTGGGGTCTAAGACCTGCCTGATC  
TGCTAACTAGTCTTGTCCCTTGGCTATAAACTGACGTTGGCACCTGGCCA  
GAAAGATGAGCAAGAGATCTCTGACACACCTTTAAGTCCCTGTGGAGTAG  
GATTATGTTGGGGAAGGTCAATTCTCTTGAAGTGAAGCAATTTGAGAAGG  
AAGTCCCATGCCGAAGTGAGAGAAGGCAGGGAATCCTGCCTAGTCAGCTA  
GASCAAAACAGTCTGCAGGACGGGACCCAGGGATGTGATCCTCCCATCCA  
AAGGCACTGAACTAAATGACTAAAATACTTTCCAGGGCTCACGTTCTTTG  
AAGAATGGGGACTAAAATAAGACAGGAGCCAGCAAGTGAGGACTTGGAA  
GGAGATGGCTCATCTGATCAGCCTCCACTCAACAATTTAATCATCCACA  
CTGGCATGGGGACACAAATGAATAAGTTGACAGGGACCTACTCTGATTA  
AGCAGTGGGCTAGTGACAGACCTGTCAAGTCAAGAGTGAGCAGGAGATGA  
TTTCAGACAGTGAGAAACAAAATTAACAGAGTCATGTCTAAAGGGTGGCT  
GGAACCTACAGAGGAGTTTAAGACTCAAGAGGTCTGGCTGGGCGCGGTGGC  
TCATGCCTGTAATCCAGCACTTTGGGAGGCCGAGGCGGGCGGATCACAA  
GGTGAGGAGATCAAGACCATCCTGGCTAACGCAGTGAAACCGEATCTCTA  
CTAAAAATACAAAATATTAGCCAGGCGTGGTGGCGGGCACCTGTAGTCCC  
AGCTACTCGGGAGGCTGAGGCAAGAGAATGGCGTGAACCCGGGAGGCAGA  
GCTTGCAAGTGAAGATTGCGCCACTGCCCTCCAGCCTGGGCGACAGA  
GCGAGACTCCGTCTCAAAAAAAAAAAAAAGACTTGAGGGAGTTGTTTATT  
TTTGTCTCTTTTAAAGACAGGGTCTTTGTTGGGCGCGGTAGCTCACGCC  
TGTAAGTCCCAGCACTTTGGAAGGCTGAGGTGGAAGATCTCTTGAGCCCA  
GGAGTTTGAGGCCACTCTGGGCAACATAGCAAGACACCGTCTCTACAAAA  
AATGTGCAGGTGAGGCTGCAGTGAGCAGAAAAACACCGCTGCACTCTAG  
CCTGGATGACAGAGCGAGACCCTGTCTCGGAAAAAAAAAAGAAAAAGACA  
GGGTCTCGCTGTGTACACAGGCTGGAATGCAATGGTGCAATCATGGTTC  
ACTACAGCCTGGAACCTCTGAGCTCAAGCAATTCTCCTACCTTGGCCTAC  
CAAAGTCTAGGACTACAGGTGTGAGCCACCACACGTGGCCTCAGGAGAG  
ATCTTAATAATAAAGGACAAATTGCCTTGCACTCCCTTAGGGGCAGGATT  
GACACATCCAAGGATCAGGCAGAAAGCCTGTGCGGAGTGGGATGAGCAAA  
GAGAAAGGCTGAGAGTTGTGAAGAGGGAGATGCAGTGCCAGCTAGGACAG  
GCCTTTTGGGCTTGGGAGGTTTTCAGAGGAGACCCACCTAACTAAC  
CCATAACATTGCAGTGGGGACCTGTTGAAGTCATGGACTACTACCTGAAA  
GCCAGAGAAATGGGAGGAGCCTTTCTCTGAGGAGGGACTCTAGTCCATA  
GGTATCTTGCCACCAATACATGGACAGGCCCTGGGGGAAGATGGTGGTA  
GCCCAGCTGGAGGAAAACCAATTTGCCACCTGAACTAGCCCAAGGTAAAGCC  
ACCCAGGCACTGAGGGTGCACACCCATGCATGCACACACAGAATCACACT  
CCTTCCTATTATCTCAATTCAGGGGTCTCAACACCCATTTTTTTTGT  
TTTGGGTTTTTTTACATGTTTACATTTTATTATTATTATTATTGTTGA  
CAGGGTCCCACTCTGTTGCCAGGCTGGAGCACAGTGCAATCGTGCAATC  
ATATTAGATTGGTGCAAAAGTAATCACGGTTTTTGTCAATTAAGTTTTG  
CCATTACTTTTAAATGATAAAACACGATTACTTTTGACGCACTTAAAA  
GCTCACTGCAGCCTCAAAATTCCTGGTCTCAGGGAACTCCTCCTGCCTCAG  
CTTCCTGAATAGCTGGGACTACAGGCACATGCAATCCTACCTGGCTAATT  
TTTTAAAAATTTTTTTGTAAAGATAGAAAGTCATTTTGTGTCCAGGCT  
GGTTTCAAACCTCTTGTCTTTGTGCTCCCTCTGCCCTGTGCAAGACCTTC  
TGGATGCCCACTAATGAAGACTTCCAGGGAGAGGAAAAGTAAACATAGGT  
CCCTGATCAAGGGACCAGGGTTTATCGACCACAAACAGCATGCCCAGATT  
CCACTGGCAGTCTTAGAGGTGCGATTTGCCCAAGTGTGTGTGGAAGGCC  
TCTCCCTAGCAGTTGGTTTATACACCAGCCACAGCACAGCATATTCTCTT  
AAATTGTGAACATTTGCAAAACTCCTTGAGGACAATCATGTCTTGT  
GTACTTTTGTGTTTTTCCCTTCCCTATGTACACGCGCGCGCATGCACT  
CATGCACGCACGCGCGCGCACACACACACACACACCCCTCAAAGTAA  
TGCTTGGTGTGCTGAATGGATGAATGGCTAATGTAAGTCATTCTAAAGC  
TACTTTCTTTGGCATACCATCACCTTTGATTTTCTCTTCTGGAACCTCCT  
ATGTTCCCAGATGAATTTGGAAGCCCTCAGGAAACATTTCAAATTTGCT  
ATATGGGAGAAATGGGAGGGTCTCTAGAAATTTACCTGCCACAGGTAT  
TTCTGGTAAGACACAGCAAAGGTGGCACCACCCATTCTCGTTACAATGT  
CAATGCCAGTCACCTTCTGTCCCATAAACTTTATTAAAGGTGCAGAA  
TCCCATGGAAGCAGGTGGACACCATCTGCTTCCAGCCAGCCAGGGGAGCA

AGGTGTCCACTGTGCCCTTGTGGCAGGAACTGCGCTTCTCTACTCTCCCA  
CTTTGAGGCCTCTGGGGCTGGCCTGCTGCCTCCTCATTGACAAGGCTGCT  
TACTGAGCAGTTTCACTTCTGAGCTGGACATAGTGCTTCTGGTGAGTCTCTA  
CTTCTATTTAACCCTAAAGATATTCTTCTTAAGGAAACGCTTTCCTGTCTG  
GGGAGGTTAGCTCCAGATGGAAGTCACAAGTGATGGCATGGTAGCTCTC  
ATCCGTTTGGGTGGATGATATTCACGGAGCACCACCATGAGCCAGTCATG  
GAGGTGAACAGTATATGCCAGCCCTGAATCAGGTGCATTGACAGCAAGGG  
AGACAAGCAAACAAGCTGAGGTTTGTGAGGATGTTCAAGACTCACACA  
GCACAGAGGAGCATCCACCACCCAGCTTGGGAAAGGACTTGTTATAGAGG  
GGGTGAAGCATGAGCTGAGTCTTGAAAGACTAGAAATTAGCCAAACTACA  
AGGAGGAGAAGGAGTTTCCAGTCAGGAAGAAGAGGTTATGCAAAAGCACA  
GAGACTAGAAAGAATATCACATTCAAGGAACTGCAATAGACAGGAAAGA  
TTGATGCGTGGGATAGGAGAGGAGGGGAGGGGATTCCAGGTGGGCCCTGC  
TTGCCACACTCAGGAGCTTGAACCTTATCCACAAGGAGGTGTGGAACCAG  
TAATGAATGGGTTTTGTGCAAGGGCTTCATGTCACCAGATTTGCTTTTTG  
GAGATACTTCTGTGGCTGATATGTGAGGAAGGGATGGAGGAAGTTTCCGT  
GGCAATCAGGAAAACCAATTAGCAGATGATTCAAATGGCCTAGGGGAAAA  
GGGAGGAGGACTTGGACTACCATGCAGCAGCAGAAATGGAGAGAAATAAC  
AGATCCCAGGCACTCAGGAAGCGCTCAGAATGAGCCCTTCAAAGAACTTA  
TGGTAGGTAGTGATGGATGGATGGAGTGTGAGTCTGGGATAGCATTGCCTGG  
GAAAATACTTTCTAGTTGAGACAGGGAAGTGGGCCAGCAGAAATGGAGGG  
CTTCTTCTTTTTGCTTTAAATACTTTTATAATATTTGAACTTTGAAAAT  
GAGCAGATATATTAGCAAAAAGCCTAAAAGGGATATTTTTGAAATCACTG  
CTAGTTCTAACATATAACTTTCAGCTTGCACACATCATCAATTAACCTTG  
ATAGCGCCTTCTGAAACTATCATCCCAAATAGCAATCCTTGTA AAAACC  
TATTTTGAAAAACGGGCCTTGTAGGATAGCCTCACAGATGTTTTGTGGTA  
GATTTTCTAACATTCTAATGTCAGGGAGTGAAAGGAATCCCGTTAGAAGT  
TGGAAAATTCTGGAATCTCTATTGATGTTTAAAGTTTTGCCGTACAC  
AAAAGTTTAAACCTTTACACAATCAGACTTCTCATTTTACATTGCTCG  
GTAATTAGAGGAAATCAGTCACCCAGAGCCTGGGTCTAGACTTGACAAA  
ATGCACCCAACAAATCCTGAGTGGCCTTGCTGAGGACTTCTCCAGAAGA  
TAGAAAACCTCAGTTCCAGCCAACAAGGGGGAAGCAGCTGAAGAAGTGAAA  
TTAACAAAGTCTTGAAGGAAATGACCAATCATCTTTGATTGTGTAATA  
ACCAGAGAGTAGAATACAGCTACGACAGACATTTTGGGAGAGAAGCATT  
TATCATAGCTTTTAGAAGAGAATATTTTTTCAGCATATAAGCACACAATT  
CCAAGACAGATACTTTCAAGGGATTGTTTTGACG

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ATGTTNNGGTTTTGGGACCCCACTTCAAACCTTCATGTTGAATTTAATCTT  
CAATGTTGAGCGAGGTCTGTGGGAGGGTGATTGGATCATGGGGGTGGGT  
TCTCCCTTGCTGTTCTCAATGATAGTGAGTGAGTTCTCAAGACCTGGT  
TATTTGAAAGTGTGTAGCACCTCTCCCTTCATTCTCTCACTCGTCACTG  
CTCCGCACTGATAGATGTGTGTGTTTTCCCTTTGCCTTCCGCCATGATT  
GTAAGTTTCTGAGCCTCCAGCTATGCTTCTGTACAGCCTGTAGAAC  
TGTGAATCAGTTAGACCTCTTTTCTTATAAATTACCCAGTCTCAGGTCA  
TTCTTTATAGCAGTGTGAGAGTGGATGAATATAGTGCCATATGTTTGTAT  
TCCCAGCTACCCAGGAGGCTGAGGTAAGAGGATTGCTTGAGCCTGGGAGT  
TTAAGGCTGCAGTGAGCCATGACTGTACCACTGCTCTCCAGCCTGGGTGA  
CAGCGAGACCTTGTTTTCAAAAAAAAAAAAAACCAAACTGTGTAAAATGTG  
TTCATAAAAGTGTCTTGCTCCACACCTGTCCCTATATATCTTATTCCTC  
AGCCTCCGACAACCTACTTTATTCACTTCTTATGTATCTTCCAGAATCAAA  
AAAAAAAAAATCAAATACAAGCACAGTGAATGTATTGCCCTTCTTCCCCT  
CCCTTTTGTTACATCAGAGTTAGCATATCATAAATACGGTCTGCATTTTC  
TTCTTTTTCAGCTATCAGCATGTTTTGGAGAGGATTTCAATTCGTGCAG  
ACAGCATGTATTAGTCAGTCCTTGCTTATAGGAAATACCTGAGAC  
TGCATAATTTATAAAGAAAAGAGGTTAATTGGCTCACAGCTTCGCAGGC  
TGTTCCACAGGAAGCATGGCAGCATCTGCTTCTGGGGAGGCCTTAGGAAG  
CTTTTACTCATGCAAGACAAGCGGGAGTGATGTCTTATATGGCAGG  
AGCAGGACTGAGAGAGAGAGAGAGAGAGAGAAAGGATGCCACATACTTTT  
AAACAACCAGATCTTGTGGGAACTCTGTCACGAGAACAGCACCAAGGGA  
TAGTGCTAAACCATTCATAAGAACTCCACCCCATGATCCAATCACCCCA

FIG. 4 (46 of 61)

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CACCAGGCCCCACCTCCAACATCGGGGATTACAATTTGACATGAGATTTG  
GGCTGGGACACAGAACCAAACAATACCAGAGTGCTTTCTCATTCTTTTCT  
ATAGCTGCCTAGTATTCTATGTCCTTTACTTCATTTAGGCAGTCTCTTGT  
TGATAGACACTTGGGTACTTCCAATTTTTCTATTACAAATGATGTGCA  
ATGAATAATTTTGGATCATTTTCCATTTACATGGGTATGTCCATCTGTG  
GGATAAATCTCCAGGAGTGAAATTGCTGGATCAAAGGGGAAGTGCACTTG  
TGATTTTCATAGTTAGCAAATTTTGTCTATAAGGGTCATATCAATTTAT  
AGTCCCACGCGTAATATTTAACAGTGGGGATTTCCCGACAGTTTGACCAA  
CAAGGTCTGTTGTTAAACTTTTGATTTTGTCAATCTGATGGGAAAATAC  
TAGTATCTCAAAGTGCTTTTAATTTGACTTTCTTATTACAATGTTAAGCA  
TCATTTTACTCTGCCAAGATCAAATAGTATTTCTTTTCTGTGAACAGA  
CTGTTAAGATCCCTTGCTCTTGTGTTGCTGGATTTTGTCTTTTTTTTT  
CAAATGTTTTGAGGCAGTTCTTACATGTGAAACAAGTTATCTCTTTATC  
TGGGGTGTGAGTTACAACACTCTTTCTCTGGCTTGTGTTGCGCTTTGAC  
TTTGCTTCTGGTGATTCCCGCAATTCTGAAAGTGACTTTTTGTCATCATT  
CATCTTTATACACCCATGCTCTTGTTCACGCTGGTTCCTCTAECTGAGGG  
CTTTTTCTTTCTTTCTATCTGGGAACATTTTATAGAGACAGGGTCTCA  
CTCTGTCACTCCAGCTGGAGTGCAATGGTGCGATCACAGCTCACTGCAGT  
CTTGAACCTCTGGGCTCAAGCAATCCTCCAGTGTGAGCTTCCCAAGTAGC  
TAGGACTACAGGTGCATGCCAGCATGCCCTGGCTGATTGTTTTATTATTT  
ATTTATTTTTTGTAGAGATGGGAGTCTCACTATGTTGCCAGGCTGGTCT  
TGAACCTCTGGGCTCAAGCGATCTTCTGCCCCCTGCCACCCAAAGTGCTG  
GGATTACAGGCGTAAGCCACCATGCCAGCCCATGTGTGGAAATCTTCTG  
TTTATCCCTTTAGGCTTGATTCTTATGTCGTTCTCCTCCCTCCTTCCTGG  
CTACTCCTCTTGTTCTTTATCTTACTCTACTTGTGATGTTACCTTGTTT  
TGCTTATAACTAGCTGCCTCTCCTATCTGAGGAGGGACTTGTGACTGTTT  
TCATCTCTGTACTCCAGGTCTAGTACATAGCGCTTGCTCAACAGATGT  
TTGGTGCATTGATAGATAAATCAATGGTAGCTGTTAATACCAGTCTTGAC  
TCCCTGCAGTGCTTCAGCTGATCCTGTTCCAGATGTGCACTGAATATCTT  
TCTGTTGAACAACAGAAATAAAGGGGATGGGTGAGGAGGATAGTCTTCGG  
TGGCCAAGGATATTTGTAGGTACTTTGCAGCACTCAGCAATGAGGAGTGG  
GCTTTAGTCCCCCAAGAACTCTCACAGCCCTGTTTGTCTTTACTGTTT  
TGTCAAATCCAAGACAAGTCAATGATCAGGAAAGACCTTTTTTTTTCTTC  
AGTGAAGTTTTATTTAGAACCAATTGAACAGTATGATATTGCTCATTAT  
AAATATTTCCCATTTAAATAATCTGAGCTTATATATTTTCAGTCTTAATTA  
AAGGACTTGATTTAAAGAGAGCACACCAGTCCAAATTGAATTGATTCCAT  
AGCTATTAATAAAGTAGGCTCTTTTACAGACACTGCTACTTCTTGCCCCCT  
TTGAATAAATTAGACCAATGAATAAAACAAACAAATAAATAAATAA  
ATAGGGAAGCGGTTGCTCATCAGAAATGTGGGAGCGAATGACAGAGGGTTT  
CTTAGAACCAATGTGGCGTGTTTCTGTGAGGCGGGCTTTAAGTGAGT  
AGGAGAGGTGAGAGAGGCTGGCTCAACAAAAGGGCTGGGGATTGGCCCT  
GAAAGGAGAGAGCTGACTGTCTGGCTGATGGACAGGAGATCCTCTTAGC  
ACTACCTTAAGGCAGGCAGTTGGGCATTGGTGTAGACAACAGGAAAGTCC  
AGGCTATAGCCGTACTCAAAAACCTTTCTGTTCCCTTTCTGCCAGCCCTA  
GGGATTGAGTCCACATTCAGCACAGGACTCTCTGGGTACAGCTCTCTTTA  
GGAAGACACAAATTGCATGGTGAAGTCAGTTATATCCTGGCCGCCTTTGG  
TCCCTCCCAGGAAGACGGGCATGTTTTCTGCTTGAGAGGTGCTGATGTAC  
CAGTTGGGGAATGGGCAGACTCAAATTCAGCTTGTTATTGATTCTAT  
CTTGTTGAAGACAAATCGCTTTTCCATCTTCTTCTTTGGGTAATTTTGG  
GATCTACACTCTGCAGCGAAAGAGAAAGAAGATTTTGTGGGGCAAGGG  
ACAAAAATGCTATGGGAAAGATGTTCTTTGGGTTGGCCAGAAAGGAACT  
GACGAGCAGGTCAATGATCAGGAGCCACACTCCTGAGTTGTAAGTGGGC  
CCCCAACTTTCTGTGTGATTATTAAGAGCCCTTCTTCTTTTCTAAAAAC  
TTAGTGCCAAATGCTGAGGAGCATAATGTAGGTGAGAATTTTTTTTTTT  
GGGGGGGTGAAAAATTAAGCTAGAGCTTCTTGAAGTACCTAGTTTCCAGGG  
GCTTTTTATTGTATTTTCTTATGGTCTTAGAATGACATCAACTTGGAA  
ATGAAGCTTTTGTGAGAAAGCTGGAGGTGATAGTGGTGGTGATTTTGGG  
AGTGGAGTGGACGTGATAATGGGACCCTTTAAGTCATCTATTTCCCAAGG  
TGTCTATCAAAATGAGAGCAGCCCTAACAATATATAATCTGTTGGGGTGT  
AACTATGGTAGGACATAATAACATCGGCAAAATGATTTAATTTTCTGCAG

FIG. 4 (47 of 61)

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CAGGATTGAAGGTTGCAAGCAGTTAAAAATTATGTTAAATTTATTTACAT  
TAATGCAAAATTTGTCAAATAGACCTGTTCCAGCTTTTCTAGGGATGGG  
GGCGGGGAGAAGGTGGTTGTCTGGAATAAGTGGTAGCAGGAGGCTGAGA  
AGGGCTTCATTCCATAGCATTCACTTACCTCCAGCTGTAGAGTGGGCTTA  
TCATCTTTCAACACGCAGGACAGGTACAGATTCTTTTCTTGAGGCCAA  
GGCCACAGGTATTTTGTCACTTCTTCTCTCTGTACAAAGGACATGG  
AGAACACCACTGAAGAAAGAGGGGTCTTGTGGTTAGGGACACAGCAGT  
GCAGGGTCACCCCAACCCCTAGGCCCCATGAGTAGGATACATGTAATTTG  
GTAGCTCTGTGGGAACCCACAGTGAGGTTCTTGGCCTAAGACACAGGA  
TAACTTGACTTCTCACAGACAATAGCAGGGTCATTTTGTGATTAGGGT  
TTCCCTCAAAGGCCTGAGGGTTTCTCAGAGCCTCATAGCAGTAGGAACG  
GAGAATGAAAGAGGGTCTACATTTTAAATGCTGAAGGAAGGAAGGA  
AGCCATTGTCTGAGTGGCTGGCAATGTGCCATCCACAGGAGCGGAACAA  
CTTGATCAATGTGGAAGGAAGAGAGGTGAGGCTGTACTTCTGCCAG  
AAATCAGGCACCAGAACTGTTTCAGGAACAGAGTAGCCCATGGGAAGA  
AACTGGGAGAGGAGAGGCTGAGCTGGGAAAGTGGCTCCAAAGAGAGACAC  
TCATTTTGTATCTTCTCAGTCACAGCAGTGTCAATTGGAAGGCCCTGGGA  
TCACTCTTACTACCCGATTCCAAAGAAACAGGATTTTCTTGGCCTGGCTG  
AGAGCAAATAGCTTCCCCCTTGAGTGAGGCTGTCTTCAAAGTCAGCAGC  
CTTAGTTGCCACACTCCTGTGCAGAGGCTTTGGCTACTGTGGCAGCATG  
CCAGGCAGATCACCACAGCTAATGATGGGTTACCGCACTTGAAACTTTT  
GCCCGTTACAGCGGAGAGATATAAGTTCTGTGGCGGTAAATTTCCC  
TACAAGGAACCACCTGGCATTGGGTGGGACGGATGTTGGGGCAAGGGGGG  
AAGACTGGGGAGGGGGATGGACACATTATCGCTCCAGCACTCTTGTTC  
GCCTCAACAACAGGAAGAGAGAACCCACAGGCAGTTAGGCCATGTCCATC  
AAATGACCCCATATTGTGGAAGAATTGACATTGCACTATGCCCAAGAGAC  
TTGGGTGGACATGGTCTTGGGAGTGCTTGAGCCGTCTAATTTCTCAGGGT  
CACACTCTGTGTTAAACAAATGCACTGGCCAGTGCAATCAAATGTGCCATT  
CTAGGACCAAAGTTTGTATATTCCTTTTTTAATATTTTTTTCACTTGTGT  
TGATCATTTGCCTTAAATTAACCTTTCTACTTTGTTTAAACATGGAGAAT  
TAGCAAGCTGCCAGGAAGCCAGGCAGGGAAACCAGGATGTTTCCATTAC  
CTTGTGTGCTCCATATCCTGTCCCTGGAGGTGGAGAGCTTTCAGTTCATAT  
GGACCAGACATACCAAGCTTTTTTGCTGTGAGTCCCGGAGCGTGCACTT  
CAGTGATCGTACAGGTGCATCGTGCACATAAGCCTCGTTATCCCATGTGT  
CGAAGAAGATAGGTTCTGAAATGTGGAGCATGTTGTTAGGTATAAAA  
TCAGAAGGGCAGGCCTCGTGAGGCAAGGTGGCAAAATTTGATTTCTTGA  
GGACACCTGAGCATATACGGTCAAAGTCTGATGACAACACCAGTAGGGAT  
GAAGCTGGGAGTGGGGTGGCTAAGAACACTGGACCTGACACTATTAGACA  
TGGGTTCAGCTTCAGGTCTATTACTGCTCACTGTGGCCGAGCAACAGAG  
CTACTTAGGTAAATGGTGATGGTCATAACACTAGCCACAGGGAGGTTA  
CGAACCTCTGGTGACAATGTAAGTGAAAGGCCCTGAGAAAGAGTGAGGG  
AGTTGCAAAATGTCACTAGCCATCAAGATCTTCTTTAAGAATAGTTTCCAC  
TAAAGAGATGATTGCTTTGTTTTCCAGCCTTCTTTGTTTTGTCTCCCCGC  
TGGGCCTTCTACCTTTAAAGGGCTTTGGCTCTGGGGGAATTGAGTTGGCT  
GGGGCTTGATGACTTCCAAGAGGACACAAGTGGAGATCTACTGCCTGCTC  
TTGGCTAACTACCTTCTTCAAAGATGAAGGGAAAGAGGTGCTCAGGTCA  
TTCTCCTGGAAGGTCTGTGGGCAGGGAACCAGCATCTTCTCAGCTTGTC  
CATGGCCACAACAACCTGACGCGGCCTGCCTGAAGCCCTTGCTGTAGTGGT  
GTCGGAGATTCTGTAGCTGGATGCCGCCATCCAGAGGGCAGAGGTCCAGG  
TCTTGGAAAGGAGCACTGCCGAGAGAGCGAGGGAGGGAGCCTGGTGAGGTG  
GTCCTGCCAGGAACCATGCTTTGACATCAGAGAGTAGAAAGCTCAGAGAG  
GAGGAAAGGGCTTGAAAGAATCCCGAGCTTCTAAAGATCATCCCTCTCTG  
GGCCAGGCGTGGTGGCTCATGCCTGTAATCCCAGCACTTTGGGAAGCCGA  
GGTGGATGAATCATTTAGGTGAGGACTTCAAACAGCCTGGCCAACATG  
GCGAAACCCCTTCTCTACTAAAAATACAAAAATTAGCTGGGTGTGGTGGG  
GTGACACTGTAATCTAGCTATTTCAGGAGACTGAGGAAGGAGAATCGCTT  
GAACTCAGGAGGTGGAGGATGCAGTAAGCCAAGATTGTACCACTGCACTC  
CAGCCTGGGCAACAGAGTGAGACTCTGTCTATAAAACAAAACAAAACAA  
AACAAAACAAAATAAAATAAAATAAAATAAAAGATTATCCCTCTCTGAA  
GCTCAAGGAGGTTAAGGGTGACTCAAGGGCACACAGCAGGTTAGAGGCA

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GACTCAAGACTAGAATG<sup>1</sup>GGGCTTTCTG<sup>2</sup>CACCTTACAGGCTATTCTTTT  
AGAATAAATCCCATTTCTACTTTGTTTCATCTTTTTTGTACATGCCCCACC  
TACACCATACATGTATACCTTCTCTATATCTTTTTGTATCCCTAATGCTG  
TCACACTATGATTTGCTTTTTCATGCAGATGACCATAACATTTTCCATT  
ACCTATGCTCACTCAGCAAGTATTCAATTTTTCTACACTGTTCTTTTTT  
TCCTTTTTTCATAACACTGTCTCATAGGCATTCTGCAAATCCTGTGAGAGT  
ACTTTTTGTGAAATGTTACCACTTTCTCTTATTTCAGAGAAGCTCCGTAT  
TAAGGCTTCACTGAGGTTGCCTTAAGGCATGATAATGGTTCAAAGGCTTG  
AAAGACAGTTAAAGAGACCTGTAAGTGCACAAAAGAAAGTTGAGCAGGAG  
AGAATTTCTTGCTGGAGCAGAGCCAAGCTACTGGAAGAGGCAATGGGGG  
CAAAGGCCAGGCAGACAAGCCAATGGGCTCCTCCCACAGCTGCAGCCAAC  
AAGTTATGCCAGTCTTAAACTTCTAAAGAAATATGTTTTTAACAAGATT  
GAGGACTGGATTATGAGGCTAGGGGAGGCTATCACAACTGGAATAAAAT  
AAAGCCAGAGAAAAGTGGCTGCCTTCCAACCTGCACAACCTGACCTAGCTA  
GGCTGATGGCTGGGCCACCTAGGAAGGCTACTGAGCATCATATAAAACAG  
AAGGGACAGCAGGAATATAACATGGCTCTTTGTAAGGATGAGTCTGAAAA  
ATGACCATTTGCTGCCCAAATGCCCTTAGCTACAACCTGAAAATATTTTCA  
AACTGGAGGTTGCAGGATGCTGGAATCTCAGAGATCATCCAGCTCAGCCC  
TTTATTTTTCAGATGAGGTCCAAAGCGGGTAAAATGACTTGTCAAGGTCA  
AACAGCAAGTGAATGGTTTTCTTTCAAGTCTCAATTCATCTTTTTGTGTTA  
TATCATCTATGTCTTGTGTTATAAGCTTCACCCCAGGTAGCAAAAAACT  
ATTCTACTCAAAAGGGGTAGACATATGTTAGTTCTCAAGATCATCTCTTG  
GTTTCAGAGTTAACTCAAGTGATTGGCATAGGCTGAATCCATCTCTTAA  
AAGGATAATCAAATTTATGTTGAAGACTTGGTTGTCTTCTACTATGAAA  
TGGGAAACATTATCACTACTCCTCCCCTGTCAACCAAGTGTGGCCACC  
ACCACCAACGTTAGTGAGTGACTGTGGTGATATGATGACCAAGTGGCCAG  
GTGACGAAGTGGTGCAGCCTGTGTCTCACTGGAAGAGGTTAAAGTCTTTC  
TAAAACAAAATACCATGGCATCAAAGTGGCCCAGAACTCCCTTCTTTGAG  
CTTTCCTGTGTTAGAGCCCTTCTTGGGTTGGGAGTTAAACCCATAGTC  
TTACCTTCATCTGTTTAGGGCCATCAGCTTCAAAGAACAAGTCATCCTCA  
TTGCCACTGTAATAAAACAGGGACATGTCTCAATTATGTCTTCTAAACA  
GGTTTATTTTTCTTCCCTGTGTACAAGACTTGACTGTTTCATAAGAACT  
GCAAACAGCCTGCCTCTCAAAGCTGCCTGAAACACCTGGCAAGTTTCACA  
GTGATATGCGCAGACAGTCCAGAAGGCAGATTCTAGGCCTGGCAGGTGG  
GCACCCTGGGTGCTCCCTGTTGGATCTTGAGGCCTAACCTCTAGCCCAGC  
AGAGTCAGCTAAATCTGAGCTCTCCCTCTCCCTCCAAGCCACACTTTGC  
AAAGGGATTCTTGTATTGTGGGCTTGAATCTTTTCTCCCATTTGCCT  
CTGCAGGAAGCCCTTGCAACAACACATCTGGATAGCCTCCAGGTCCCAAG  
CTGGAGGGACTTGTAAATGGGAAAGTAGTCTTTAAATCAGATTTACTTGG  
CACCCTGTTTGGCACTGAAAGAGGCAATTTAGGGGAAAAATCTGGTCTCC  
AAGCATGATAACACTCTACTCTTGAAGAGGAGACCTGTCTCATGTTACT  
GGTCTCAGCGTCTCCACTGACCTGTAATAAGCCATCATTTCACTGGCGAG  
CTCAGGTACTTCTGCCATGGCTGCTTCAGACACCTGTGTAAAAAGGAGAA  
AATGAGTGACTTCCCCATGACGGCTACGTTTCATGTGTGATTTCTCTCAGC  
ATCCAGTGATGGCAGTCATGCAAAGAAATGATCTCTGAGTAAATGAATG  
AATGTGTGAAAGAGAAGTCTTTGGGTCTAGAGAAAAGCATTGCTAAAC  
CAAACCCCACTAGCAATGTATTGGCTAGGAGAGCTGGAGCAGAGGCTTT  
GACACTAACCTTTAGGGTGTGAGCTGTTAGATAAGCAGTATCCATTCCCA  
GAATATTTCCCGAGTCATAAGCATTATATTACACCTGGCATTTTTGCAA  
AAGCTGAGAGAGGGAGGCAGAGAGGGAAGGAGAGGGAGAGACAGAGAAAG  
AAAGAGAGAGAGAGAGAGAAATATGCATACACACAAAGAGGCAGAGAGACA  
GAGAGACTCCCTTAGCACCTAGTTGTAAGGAAGATTAAAGTCATACTTGA  
GCAATGAAGATTGGCTGAAGAGAAATCCAGAGCAGCCTGTTGTGCCTTGT  
GCCTCGAAGAGGTTTGGTATCTGCCAGTTTCTCCCTCGCTGTTTTATAG  
CTTTCAAAGCAGAAGTAGGAGGCTGAGAAATTTCTCTGTTGAATACCTG  
ATTTCACAATCAAGTTAAAGGAAAGGGGAAAAGAGTATTGGTGGAAGCTT  
CTTAGGGGAGGGGACTAATAAACTGAGATAATTCTCTGGTTTCATGGAAGG  
GCAAGGAGTAGCAAACATGACACATTTTGCAAATGTATCACCATGCAAA  
TATGCAATGTTTTCTGACAATCGTTGTGAGTTGATGTCCACATTAATA  
TACTGGATTTTCCACGTTAGAAGAATGTTTAAATTTAGTATATGTGGGA

FIG. 4 (49 f 61)

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TGGGTTAGTTCTTATATTATTGTGTGTACATGCAGTGATGTCTGTTCTTT  
GTAGTGAGCTGTTCCCTTCTTGTTCACCCCTCTTGCTTAGAACAGAACTAA  
SCAATCTGCCCCAACATTTTCCCAATTTCCCATCTCATTCTTGGCACT  
GGCTTCCTAATATTTGTCTTATGAGTCATTTTCTTGATCATTTCATG  
AGTCCCTCTGGGATCTTAAAGTATGAAAAATGTTGTGTGTACCCACACCT  
GTCTTTGTGGATATTTCTCTCCTTTCCCTTCTGCTTCTGGGATTATTTGG  
GAATGGGCACATATGATTTTATCATATCGCTTCCACTTCTTTATGGCAT  
CATCTCCAATGGGCTTCTTCTCCCTCTTGGATCCAGGTTCTCAGATTGGG  
GACATGCAGAGTCCAAGGAACATTCCATTCTCCTCCCTGGTCTAGAACAA  
GGAGGGCTTAGATATATGAGCAGGTGGCTGGGGCTGGCGAGCTATGTAGT  
CTCCAATGGCTTTTCCCTGATGTGCGAGTTGTTATGTCAAGTTCTGGGAGA  
CCAATAAGACCTTGTCTTCTTGGATCCATCAGAAAAAGCCCCCTGGGT  
GGGTAAGATGGATGGCAGGGCTCTCCTACTCTATGTCTTTTCTCACACCT  
AGTGGGTATAAGAGAGGGGACCACAAACAGAGGGGGCTCTGGTACCACTT  
ATCCAGGGTCTGGAAACATTTTCTGTAAAGGGCCAGATAATAAATGTTTC  
AGGTACAACCTCAACCTTGCATCATTTAGAAAAGCAGTCRGATAATA  
CATAAATGAATGGGTGTGGCTGGACTTGTCTGCGGTCCCCTGTCTTATA  
TCATTGTATTATATCATTTTTTCTTACATACAAATTTAGAAGCAATACTT  
AAAAAAAAAAGCCGTCCTTTATTGAGCACCTACTAAGTGCCAGGTACCT  
TTTTTCCCTCATTATCTTATTAACCTTCTCATAATAACCTTTAAAGTAGA  
TAATATTGAACCATTTGACCTATGCAGAACTGAGGTTGAGACAAATAAAT  
TATTTAAGACCCGACAAACAGTAAATGCTGGAACCTACGACTCAAATATGG  
GTAACTGAACCAAAACCAGATCTTATTTCTCACTTTTAATTGTTACAT  
ATGTTTATTGCCTCATCTCCTGTCCACATGGTGCCCATCGGCAGACTCCT  
TTCTCATCTCAGTGATTGAGTGACATTCTAAACTACATTGGCCTGGCAG  
ATTCACCTCTGTCCCCTAAATGTTTCCACATTGTCTTTTAGGATTGAGA  
TCCTCTCTGTTCCTTCTTCCCTCCTTTCTTCTTCTGGCGGTGACGTG  
CTGTGTGAATTTGTTTCTTCTCCTCTCAGGGTAGTACTGGGACTTTCCA  
AATCAGGGTTTTTAATGATCTCTCTTCTTCTGAAATTTCTTCTTAT  
TCCCATTCATTTCTCATCTATAAGTGGCANCTTTGTTGCTGGAAGATAT  
CCCTTGTGCAGGGATTNCTCTTTAANAATTTGTCNNNACC

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GTGATCGTCAACCTCCACCCCTGTAGGGCCTCAAGCATTGAGGACAATCA  
CTGGCTGCCCCAATAACCCAGAAATGTTGCCGAGACAGGAGGCGGTGGCCC  
AAGTTCTGGAATGGGGTATTATTATGTACGACAAAGGCCTTTGCACAA  
ATGAAGGCTTTAAAAATGCAGTCCTAGTCAGGTGGAGGAGGGCTTATAGG  
ATTCCCAGGAATCTGGATCATTCTCTGAGAGCTTTCCCTTGTCTCTGTT  
AAACTCACATCGTACGGCCCAAATAACAACAAAAATGGATGTAAATTC  
TTGAAATAACTTGTGGATGGGGGAACAAGGCCACCCCCAGATCTGCCA  
GAAGCTTCAGGTGAGGGTCCCAAATGCCAAAAAGTCTGGTATCAGAGAGG  
ATGGCCAGTGACNTGGGGACACATGCCCTTTGCTGTGTCACTCAAGGAGC  
AGCAGCTTCGGCCCGCACAGTGACCGAGACCCTGGCTTCCCACGCTGGG  
CAGGAGCTGGTGTCTGATGAAGGGAATGCCTGGCAGCACGTGCTGTCTGT  
CTCCTCGTGTGAGCTTACCTGGCTTTGCTGCGAAGAGGCCACTTGCATTT  
CTTTATTTTTTATATTTTTTTAATTTTTTAAATTTTTTATTTTATTTTA  
TTTTTATTTATTTATTTATTTTAAATTTTTTTTTAATTTTTTAAATTATG  
CTTTAAGTTTTAGGGTACATGTGCACATTGTGCAGGTTAGTTACATACGC  
ATACATGCGCCATGCTGGTGCCTGCACCCACTAACTCGTCATCTAGCAT  
TAGGTATATCTCCAGGTTAATCCCTCCCCCCTCCCCCACCACCAAC  
AGTCCCCAGAATGTGATGTTCCCTTCTGTGTCCATGTGATCTCATTGA  
ATTTCTTTAAAGGTGGAATCTCTCAGTGGGGTCTAATCTGTTCAAGAAATA  
TCAAAAGAGTATCCTTGGGAATGACTGGAATTCAGAGTCATCTGGTAAT  
CCTCATAAAACAACCTTGGATGTCTCTCAGCACATCTCCACCTTGAAC  
GCAGGAGGCTGGTTCAAATGGAGGAGCATCGCTCTACTGCATTTTTTTTT  
TTTTTTGGCCTAAAGTGCAAAAGGGGATACGTTTTCATGTAAATAAATCAA  
CTGCAAAATCGCTAGTTATGCTGAGCCCTGTCCCGTGTGTGGACACAAAG  
GAACCAAAAGGCTTTTCTCCCGCCCAACACACACATAACACACACACAA  
ATCATAAAACATACATACCCCAACACATAACACACACACACACACACA  
CAAAATATATACACACACACACACCAACATGCCCAAAACCTGTGTCC  
AAAAATAAATCTACTGGTGGGTTTTGTGGTCTCCCTAACTTCAAAATGA

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AGCCGTGGACCTTCGCACTGAGTGTACAGCTCTTAAAGATGGCATGGAT  
CCAAAGAGTGAGCAGTAGCAACGTTTACTGTGAAGAGCAAAAGGACAAAG  
CTTCCACAACCCAGAAGGGGACCCAGCAGGGTTGCTGGTTGGGGTGGCC  
AGCTTTTACTTCCTTTTGGCCCCCTCCCATGTTCTGTTTCCATCCTATCAG  
AGTGCCCTTTTTTCAATCCTCCCTGTGATTGGCTACTTTTAGAATCCTGC  
TGATTGGTGCAATTTTACAGAGTGCTGATTGGTGCGTTTACAAATCCCCTT  
GTAAGACAGAAAAGTTCCTGATTGGTGTGTTTACAAATCCTCTTGTAAGA  
CAGAAAAGTTCCTCAAGTCCCCACTGGACCCAGGAAGTCCACCTGGCCTC  
ACCTTTCAACTCCATAATGGCATGAAAATACATATGTTGTACAAAACATA  
CATACACAAAGTATACATGCATCTCCCCAAATATACACATACCACAGAAA  
CATACACACAGGAAGTACAGCTACCTGTCAAAAGTCTGCATGGTGATTGCC  
TCTGCAGTGAAGTGTAGAAAAGTGAATTTGTTTTCAATAAATTGGAGT  
CCTTAAAGATCGTTGTAAAGATAGAAAATTTTAAAGTATATAAAATAAA  
ATATGTATGTCCTTTGGTCTAGCATTTACACATGTAGGAATTTATCCTAG  
TGGAGTAATCAATGATATATGCAAAGATTGGACAAGCATATTAAGCACA  
GAATTATGTATGCATATGTGTGTATATATATATATATCTCATACATAT  
AATAATGTAAAGTGAAAATAACTCAGATGTTCAAAATTGAGGATTAGTT  
AGACTATGATCTGTCCATATGTGACATACAAGTTAGCTGCCCTTATTCT  
CTCGAGCTTCGAACCTCCTATAAACAGTGTCCCTTGTATATCAGTATTGGT  
ACAGATAATCGAATTTATGAGGTTTTACATGGGGCAATAAAGGCAAGAG  
TTTATGAATACTCCATACTACACTAGGTAGCACCCCTATTAAAGACAAA  
CTCTTCTCTCTCATTTCCCTTCCTTTCCGGAACCACTTGGTTGAATCTCT  
ACAAGTCTCTATTGCAACTGCCTCAACATGGCACCCCTCCCTGCATCTCCA  
TCTTCCCTGTCTGAGAGCAATGGCCTGCTGCCCCACACTCACATCCTC  
ATTCATTCCAGAAGTGAGCACCACAGAAGTGCCTACAGTTACCCCAACCA  
CCTTCTTAGAAGATAAGTTAGTGTGTTTGTGACTTTTTAAATTTTTAC  
TTCTCTTTTTCTTCAATCTCATCCCATCCCAAGAGGTTTATCAAGAA  
GTTCTCTAAAGATATGTGTCTCTTATGGAATTTAACAGAAATCAGGGAT  
TTGTATTCTAGCCATCAAGGGAATAACATTTTTCCAGGTCTTTAGACAAA  
TAATGGAATACCTTGCAAGTAATTAGATACACTATTGTAGAAAAGTATTGA  
TGAAATGGAACGATGTTTGAGATATCATATTGAGTAGAAAAGGCAAGATA  
CATTAAAGTAGGAAATGTATCTTACAAAATAATTTGTGACACACTCCTA  
TATTTGTATGTTATATAAATGCGTATGTGAAGAAAGGCTAGAGGATGAGA  
CCACAGTCTTCGGTGAAGTTTAAAGAGATGAGGCTGCAGCATGCTCAGAAA  
GGCCTGGGTATATAGTTCCTCCAGTAATTAAGGATGTGATCTTGGGTAAAT  
TGTCCATCCTCTCTAAACTGCACCACCTTTTGTCTGTAAAACAGGAAGGA  
TGGTATTTACCCCAAGGGTCATCAAAGGATTTGGTTGGAGAAAAATAAAT  
AAATGGGCTGAGCCAGACCTGGCACAGTGAGAGCACAGTGGTTGACTAT  
TGTGCTGGCCTGTTGTTCTGTGTTATTGACATGCTGCTGGTGGTGGTCC  
AGAAGCTATTACCTTAATTGGTTATGTGGATTTCCCCTCATCTGAGCAG  
CTGTGTGTGGTGTGTTGTAACATAGCCATACACAGTAAGTACAAAGGGCA  
AATGTGATGGAAAAATGCAAGGAAGTGCAGATAAATAGCTAATGGGCTGT  
AGAAGGAAGCTAGTCTTGGAGGGCTTGATCAAGGAAGGTCCTTTTGCAT  
GTCACCTTTGAAGAAGAGGGGACATAGAAGAGGTATAGTGCATCCCGGAG  
TGTACCTGGAAGGGAACATGAAAAGAGGACATTTTTCTCTGGGACATGGG  
GACTCCACTTGATGAAGTCTGGAATTGGGGCAAAGAACCATCATGAGAA  
CAAGGGCTTCCTTGAACCTCCCAGGCTCATTGGCTGATCTAAACCCTGTG  
TCCCCTCTTTCTTCACTCTCCTCTGTTTCTATACCTGTATTATTGGAC  
TGGACTGGAAGCCACCTGATCTATCAAAAGTACCTTGAAATGTGTTGAAT  
AGGTGTGGCACAGTCTTAGCAGAGTGGCACTACCCCAAGGAATTTGT  
TTATACCTTTGGCATGGAATAAGCAGGAAATGAGTGCATCACTGATAACT  
GAGGATGCTATTTATTATTGGCCAAAGGAATACTTGTGTTGTATTTGCAT  
AACCCTCACAACTGTTGATTACAAATGAGTACCAGACCTAGCTCCTTC  
AAGTAAAGGATCCTGAGAACTGAAGGCAACAGAGCTCCAGGAGTCCAAG  
ACAGAGCCACAGACCAGAGGATCCCTGGGCCAGGTAGGTGGTCTCTCTG  
CACTGGCTTTCAAGGCCAACAGGATGGATGGGGAAGTAGAGTAGCATCTG  
GCCATCTAGACCCTTGCTTTTTATCCCCACTGGAAGCACATCTGAATTTT  
TAAATATGATCTCTGAGACCTGCCAGAACACCTTGCTCTCAGCCCCAGT  
AGCAGCCTGCTCTCTCCAGGAGGGCTTCCACTAACAAAGTAGGGCATTGC  
TGGAGGGCCAGGCAGACACTAGCTTAGGAAATCCACCAACCCTGGAAATG

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CTAGTCCCTTCTCTGAAGGCTCAGAAGCTGACTTTAGAGTCTAGAAAAT  
ATTGGTCTTGGGAACAGATTTTGGAGTCAAAGAGATGGACTTCAGATGG  
CCAGATGCACTGCTTCTTTAGGGAATTCTGTGAAAGCTCCCTGCATTTAT  
CTTAATACAGGCAGCAGATTTTCATGAGTACCCCGAGGGATGGCCCCAGG  
TCCTCCAGCCTGTGAGCATCCTTCTGTCTTCAGCAGCACCACAGTATCT  
TTATATGTCTTTGGATACCTACGTTTCTGCCAGACATCTCTTGCTCTGAT  
GCTCTGGCTGCCAAATTCTCTGTCAAGCGCTCCAATTTTTTGTGTCTCT  
TGATTTACCCCAACATGACAAAGGCAGTTGTGCTTCATGTATTCAGGGAT  
ACTGCCAAACCACAAACAGGTTAAAATCAAATAGCAGATATCCCTGTTCC  
TAAAGACCCATCAGCTCTACCCACCTGCTCCTGCTCACCCTCCTTATTGT  
TGAGTCTGAAGCCCTTCTTGTCATTTTTATTTTTTGCATGAACAATTT  
AGTTCCCTTGTCTCACTCCTAAACCTTTCTCAAAGGATTGGATTTGTAC  
ACAAACTGCCTATCTCTGCAATCTTAGAAGTGATATGATTCTGAACAAAT  
CACTTAACCTTTTGTATTTTATTGGTAAGATGGGAATACCAATTTTTGCT  
CCACTTCTGTCTATGTTGGCCTGGGCTGATGTTGAAAGCTCTCGGTCAA  
CTGAGATAGGGTGTGCAGAATTTATATATATAAATATATCTCTCCAACC  
CCTCCCAATGAAGCAAGTCACGTGAGTCAATCCTACCCTAAGATATTAGG  
GATTGAGCCTCCTGGGACATTTGGTGGCTTAGGTTTTTCATGAAAAGAGGT  
TGCAGAGCAACTGCTTTTTGTTAGGCAAAGATTAGGCTACTGCAGAGACT  
CAGCAAACTTCTATAGAAGGTGTGAGATGGTAAGTATTTAGGCTTTGCT  
TGCCAGATGATCTCTCACTAGTTAACCATGCTATTGTAGCCTCGAAGCA  
GCCAGAGACAAATATGTAAACAAGAGCATGGCTGTGTTTCAATAAAACTTT  
ATTTAAAAAACAGTCAGGGACCGGATTTGGCCAAAGGCCATAGTGTGCC  
AGCCCCAAGACTAGAGCAATGCACTTTTAACTTTTTTATTTTATTTTGT  
AAAATGCCAAGATCCACAAAAATGCTATTGCACCCCGTGTGTTAGCACTG  
TGACTCAAGGTTTGGGAAATTCTGCTTTGAAGGCGTGATAGACAGGAGAG  
CATGGTCTGGCCCCCTTGGTGCCTTTCTGGTTGCAGCGAGCATTTCAAAC  
ACAGGCAAGGCCAGTGGTCTGTTGAGCACTAGAGACATGCAGCAAGGTG  
TCCTGGGGTGAGAAGATGCCATAACTGGTCCCCCTTTCTATCTCCTTAGGT  
CTTGGACTTCATTCCATTTTCTGTTGAGTAATAAACTCAACGTTGAAAAT  
GTCCTTTGTGGGGGAGAACTCAGGAGTGAAAATGGGCTCTGAGGACTGGG  
AAAAAGATGAACCCAGTGTCTGCTTAGAAGGTAAGGTTCTTGTAAGAAATC  
TACCTCAGGGCCAAAGTGTAATTCCTAGAGCAGAACTTTGCTAGGTGCTG  
TGCACAGACCCAGTTGTTTCTGCTGACTTGACAGTAAGTGAGCTTTCA  
AATTTCCCTGGACAAATAACTAGACAAGAGAAATTCTGGAAGAGAAAAGG  
AAGCTTTGCTTCAGTGTCCAGGCACATCAGGTAGTAGATAAAAGGATCGT  
CCTCACCTACAGATTTGGGGCTTTAGCATCCTGTTTGCCAACTGGATGGT  
TGCATATGCTTCAAATGCACCTCTTCCCTCCCAACATTCCCAAGTGGAA  
GAGAAGCCTCCGATGAGAAGGAACCTCTCTAAGGCTGGGCTGAACAAATGA  
CCCAGGCACAGGGCATCTGAGTATTCATGAGGAACACATTTGGGTGTTG  
CCCATGGGGGCAATAGGAGGAGGCTTTTGACCCAAATGATTGTCTACTG  
AGGTGTGACGGGAGAGGCTGTGACATGCCAGAGGCCAAACCCGTGATCC  
AGTTTCACTCTTATTCTATGTTTCTGAAGAGGGAAGCTATGATTTAATGTC  
ATTACTATCATGCTGCTCTAGTATTTCTCAGCACATACACAGAAGAGGGA  
ATTAAATGGTCTTGATACCCCTAAATCCTTGGAAAATCCGAATTGCATA  
TGCTAACCTCACTGCGTCTGACTGCAGACCCGGCTGTAAGCCCCCTGGAA  
CCAGGCCCAAGCCTCCCCGCCATGAATTTGTTCAACAAGTAAGGCCTC  
GGGGTGAGGTGATGGGGGTGGCTGAGGTGCGAGGGTGGGGATGGGGGATG  
GAGCCATTGGGTCTTACAGGGTGAGAGAATTGTAGAATGGGGACACC  
TAAGGGTGTGGATGGGGCTGAAGTCTTTCTTTGTGGAAGCAAATCCCA  
TTAGGAGATAACTCTGGGAAAGATGAGCCCGGGGAGGGGCAGGTGATGCT  
CACCTGCTAAGAGGCAAAGGGCAAGGAAGAGTTTGTGCCTGGGAACCTTC  
CAGGTGCTTCTTCTGACCATAGCCAAGAGACTGGAGACACAGACCTCCTC  
CCAGCACTGAGGACAAACAGCCATGGGGCCAGTGGGGGTGCAGGGACACC  
CACACCACTAAGGGCTCAGGGCGGCGCCTTCAGAGCCTGAACCTTCTCT  
CATGCTGCCATTTGAACACCACAACACCCTAATAGGAACTGTTAACATT  
GCCACTGTTTCAAGTGTGGAAACCGAGACAGACAGTGGAGATTCCCTGCCC  
TAGGTGACACAGGTAATAAGTGACAGATGTGGAAATTTAAAGGTACTATA  
ACGTCTGTCTGCTGACTCAGGCTTAAGGCTCCCATCACCTCCTCTCTC  
AGGACAGAGTCAGGAGGCCTCAGCCTGAGCCCCAGCTCTAGTGCAGGTTT

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ATGTGGGAATACTGAGCCTCACTAGTALATGGCAGAGAGGACCAAATGG  
GACCAGGTGTGTAAGGGTGCCTGGCACAGTTGGGGGAGGCTGCTGTGCT  
TCTCCACCSCTGCTGCTGCAGTTACCTTTGATGTTTTAGTTTTGTTGTAG  
TTACACCATTGCTGGCTTTGGATCTGCACTGTGTCCACTCCAGGTGGAAC  
CAGGCACACAAGCCTCTCTGTGCGGCCTGTCTGACTTCTCCTTGTGAGG  
GCTGGGATCTCCTTCAAATCTGGCGGAAGTGGTCTCCAAGTCTGGTCCT  
CAAACGTGAGCAGCATCAGCGCCTAGAAGTGTAGGAATACACATTCCCA  
GGCCCCACCACAGACCTCCTGCTCAGAACTCAGGGCGCTGAGGCTCTA  
GGGGCTGCTTTAAACAAGCCTTCCAGGTTATCGTGACGCACCTTGAAAGTC  
TGAGAGCTACTGCCCTACAGAAAGTTACTAGTGCCCTAAAGCTGGCGCTG  
GCACTGATGTTACTGCTGCTGTTGGAGTACAACCTCCCTATAGAAAACAA  
CTGCCAGCACCTTAAGACCACTCACACCTTCAGAGTGGCCTTGAGAAAGA  
TTTGGGGTCAAGGATCATGAGCGAGAACACCACTTAAGAGGATAGTGAAC  
TAGTCTGCATGTGAGCGCTGAGATCCTATGTGAGGCTGTGATAGGAGGG  
AAACAGAAACCAAAGGAAAGAACAGCTTTAAGAAGCGCTTAAGAGGTACA  
AAGTAAAATGATGGTGTCTAGAAAAGTAGCTTCTTAAAAAGAGCATTTC  
AGTCTCACCCCTGGACTAAGTGAATGAGAATCTCAGGAGTGTGAGGCCAG  
GTATCCATGGTCTTAAATGCCACCCACCAGGTGATTCCCAGTGTGCACC  
AGGGGTGAGAGTCACAGCCTTAGGCCATGCCACTCAAAGGGTGTCTTCAG  
ACCAGCAGCACCCACAGCTCTGGGAGTGCATCAGAAAGACAGAGGCTTGG  
CACCACCCACCACTACTGAACCATAGTTTGCAGGTGATTCTTGCACATT  
AAAGTGTGGGAAATGGAAAAGCTTAGAGTTGAGCTAGCTCGGTGACTCTC  
AGTCAACCTGCACCTGCTCCATGAAGTCAAGTGCCTGGGATGGGCCCAG  
AAAAGCTCCTGAGGAGATTCTGATGTAAGGCAGGGCTGATAACCATGGAT  
CTCATCTGACCCCATATCACTGGGGAGTTACTTAGGATCTTGCCTGGGGC  
CAGTCATCTCTTCCATAGACACTGAGAGTGTCCACGATGCTTGGGGCACT  
ACAGGGTGGGAGGTGGAGGATCACGGGTGAGTCAGATAGGAAGCCTGCTC  
CTGGGGAGCTTACAGTGTCTATAGGGCAGCAAGCCAAGGATGCCAATACCT  
GTGTGACGGTACCCTGACGAGTGCAGAGCGCTGCAGCACCCAGAGAGGAA  
GCTACCCCTGTGCAGAGGGGGCTGAGGAGGGCTGCAGGGAGATGACAGGAA  
AGCCGGTGTACAGGAGGAGTCTCCCCACTCTTTGGGCATGAGGAGACC  
AGGAGGACATTCTACAGTGAAGAACCCAGGCAGAGGCCATGTGCTTATGG  
CATGGGAAAAGAATGACACCTTAGACTTATTCTCTACATTAGAATTGCCT  
ACCACAGATACCCATATTATAGCTTACATAGTGTGGTGGTTACTGTGTT  
TTCATATTGTACATTTGCCATTTTCAGCCACCCACCCATTCTTGACAG  
TCACTGGCCAGCCTGGGGGGCCCTGTTCTTTATCAAACAAGTGCCTGAG  
CTCTTTGCAGAGGTGAGGGTCACCTGTCCAATCAGAGGCCAGGAGGGAAC  
GTTCCCTTTTAAAGCCCTACTCTAGGCAGGCCTGGCCCAAATGAGTTGCT  
AGGAGCCCACGCCCTAAGAACCCTCTGAGCACTGTTGTGGCTGGTCCTGC  
TGCTAGAAGTTGTTCTCCAGGGCCAGGTGCAAGATTTGTGGCTTTTCAA  
AGGAGCCACTAAAGCTCCAGCTCAGCCTTGACGGTGTGGGCTCCTGGG  
GGCTTCTGCTCCCAACCCTCCCACTCTTCCATCACCGCTCCCTTAGCC  
TGGCCAGTGCAGGGATCTGTTCCACTCTAGGCACTGCTGAGGGAATGATG  
CCTCCAGTCAGAGGGTGCAAAAAGAGAGTTAAGAAAAACAATGATTATA  
AAAAGTCTTTTTATACGCCAGACATTTTCTTTGCTCAGGCTAAGTGCTA  
CTTATTTGAGTAAGCATTTTAGTTCTCATAACTCCTCTCTCAAGTAGGTG  
CTGCTATTACTTTTCAATTCACAGATGAGGACATTGAGGTTTGGAGAGACT  
TAGTAACTTGTCTCTGTCTACAGCAGAGCTGGGATTTGAATCTATCTG  
TCCAAATCTGGAACCCATTGCTTGACAGAAAGCTTAATTGCTTGTCCT  
AGCAAGATAGAAAGCCTGGGAGTGAAGAAATATTAGTGGCTGTGATGT  
CTGAGCCACAGGCAGGGTGGAGAGCTAGGGCTGGGGCCCTTGGACGTGG  
GGAAGAAAGGGCTGAGTCTTCCATTTTCAATGTGAAGTGTGATATCTGG  
TGATATTGATCTAGGTCCAAAGGTGAAGAACTTAAACCCGAAGAAATCA  
GCATTATGACAGGATCAAAAGTACTGGTCTGGAATCTGGAATCTC  
ATAGCAGTTCCAGATAAAAACTACATACGCCAGGTGACTCTCAGTTTTG  
GCTGTGTTTTCTGCCCTCCACCTAGCAGGGGTAAAGCCTCCTGCTAGGTGG  
GCTCAACTCCATGCTATACCATGCCCCATCTCCAGCAGGTGGTGAAGCG  
AGGAGGAGAGGCCCCAGGGACTAGGGCATCAGATGAAGGGTCTCTAGCAA  
TGACCAGATCTGAAAGTAGTCTTCTGGAAGGGCTGGAGAAAAAGAAGGA  
GGCAGACACTTAGACTGGAAGAAGAGGAGGCTTAAACCGGTGTGATGGAG

FIG. 4 (54 of 61)

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AAAGCTCTGATAAGGTCAAGCTCCTTCTGTTTCTGATCCTGATGGTGATGG  
TGATCAACACCAGCCAGTGCACAAAAAGTACATAGTATATTTAGTAGAT  
GTTTCCACACAGAGAAATGGTAAATATTCAAGGCGAGGAATACTCCAAA  
CATCCTACCTTGATCATTACACATTCCGTGCATGTAATGAGTACTTGCA  
GTATGCCATAAATATGTGAAATATTATGTATCACTATATAAAAGAAAAA  
AAATGTGGCCAGGTGACATCCATATTTTGGAGAGGAAGGCATGTCTTCTT  
CATAATATCACAAAATATTTTCAACAAGACACAGCTGTTCAAATTA  
GTCTCTGAGCCGGGGCTGTCTCATGGCAGTGAGGACTCTGGTTCCCTTAC  
AGACTAGCAGAAAGGAGATGGGGCTTACTGACCATGGCCTTGAGGAGGCT  
GAACATGCAGGCCAAATGGAGACACAGACAGCCTGGGCTTGGTCTGCTC  
CATCCCCTTCCAACTGATGAGATATAGTGAGTCACTATGACGTGGGTCA  
CTCATGCTTCCGTGTGAGGCTCCACCAAGACAGCAAGTGCATCAACACCTT  
ACGGAAGCACAAAGGCCCTGTTTGTGTTGACTTCATGAAAGGCATGGTTG  
TGGTGATCGCATTGAGTAGGCTTTTGGGTGAGAGGTGAAAAACCCCACT  
ATCATGCATTGCAGCCCTCTGGTGGAACTGTGCTTCAGGCTCTAAATTT  
CAGGCTCTAGACTGACTCCAGGATGAGTATTTGGAAGCTGAAGTCAATCT  
GTGGTCTCTTCTCCTGTAGAGCAGGAGTCAGCACTTTTCATAGAGTGCCA  
GATTCTATATATCCTGCCACATGCTCTGTTGTTACAGAACAAAGAAGGCC  
ATAGACAGCATGGCTGTGTTGGCAAATACACAAAACAGGCAATAAGCTGT  
ATTTGGCCTTTAGGCTGCAGTTTGCCAACCCCTGCACTAACACAGAGCTT  
AAAGGTGGTGGTGGTGTGCTGGAGCTAGCTTATATCAGCTTGCAATAGCC  
AATTGCTAACATCTCTTCCAACTCTGTGTCTGTGCCTTGATGTTGATAG  
TTTGAAATTGGCTACCCCATTTAATGCTGCAATCTTTTCTCAGCCAGCA  
CTACTGACTCCCTTTGCCCTGTCTTATTTTCTCACTCTAACATGCTGT  
ATAGTTTCTTCTTACATTTATTGTTTGTGTCTTCCACTAGCATGTATGT  
CCCACAAGTTCTTTGCTCTGTGATGTATCCCAAGAACCCACTGCAGTGCT  
TGGCACTTGTAGGAACCTCATAAGATTTTTATAAATGAAGAAAGGAAGAA  
AAAAGAGAGGGAGGGAAAAAGGAAGGAAGCCTTCTATTTAAATGATGGC  
CTTCTCCATATTTCTATAGTAATATGACTTCCCTTGCAAAGGGGGATGCA  
TTTTGGAAAATGTGTATAAATAAACTCAGGTGGTTTTGAATTTCAATTTT  
CTAACTGTAATTGTAATCATTGGTCTTTATGTTTAGTGAAAAAGTTTGG  
CCCTTATGCCTCACACCTGAGAAATCCCAAAGTATTGGTTTGTAGAGCTC  
CCATAGAGAACCATAAACTGGGTGGCTTAAACAACAGAAATGTATCGTC  
TCCTGGTTGAGGAGCAAGTCTGAACTCCAGGTGTTGGTTCATTCTGA  
GAGCTCTGAGAGAGAATCTGTTCCAGGCTTCCCTTCAGTTTGTGGTAGCT  
CCAGGGTTTCTTGGCTGGTGGCAGCAAACTCCAGTCTCTGCCCCATCT  
TCACATGACTGTCTTCTCTGTGTTTCTGTGTCCAGATTGTCCTATAAG  
GACAGAGTCATACTGAATTAGGGCTCACTCGAATGACTTCATCTTAAGTT  
GAACTGTATCTGTAAAGACCTTATTTCCAAGTAAGGTCACATTCACAGCT  
ACTGGGGGATAGGACCTCAACATATCTTTTGGGGGACATAATTCAACTC  
ATAATACCCAACATGATAACTGTTTATCCCATGAAATTTAATGTCTCTCA  
AAAGGTGATCTCAGGGCATTTAATCTGTGACAGAACTCCCATAGGAAAC  
ATTCCAACCAGAAGCTCCTTTACAGCTGGTCACTCCTCCTACCCCATCC  
GAGGTCTCTGGGCAGGGTGAGGCAGGTGGGGACAAGAGAAGGCTGTCTC  
GGGTGTAGAAAGAGAAGACCTTATTACCCCGCACTCTGTTTATGAATG  
AGCTATCCAGCATAGGATATAATAAATCGCTTTAGGAGTGGTAGACTCCA  
AACATTTTTTGGTCCAGTTATCCTAATCAATTAAACAACTCTAGAAC  
CCATCTTGAAGTGCAGGCATTGGGACATTATGAACTTACACAGAATTCA  
AAAAATTTACAAGGGCTAAATAAAACAGGGTCTGACATCTAATATTTTCTT  
CCCACATTTCCATGCACTGTCTGGCTCAACCATCCCCAACCTCACTCTC  
ATCCTGGTGGACACATGCCTAGTGATGTGATCAGCTGGTTCACAGGGGGC  
TGGTGATGGTGGATATACAGCTTTTGCCAAATTCATGGCATAACTACTC  
CAAATATGGCCAAATTTCAAACACCAACATGAAGGCACAGACACAGAGTT  
TGGAAGAGATGTTAGCAATTGGCTATTGCAAGCTGATATAAGCTAGCTCC  
AGCACAGCACCACCGCTACCTTTAAGCTCCTTGTGTTAGTGCAAGGGTTG  
GCAAACCTGCAGCCTAAAGGCCAAATACAGCTTACTGCCTGTTTTGTGTAT  
TTGCCAACACAGCCATGCTGTCTATGGCCTTCTTTGTTCTGTAACAACAG  
AGCATGTGGCAGGATATATAGAATCTGGCAGTCTTTAATAAGTGCTGACT  
CCTGCTCTACAGGAGAACACAGATTGTCTTCACTTCCAAACATTCTCT  
CTGAGTCAGTCTAGAGCCTGAAATTTAGACTGAAGCACAGTTTCCACCAG

FIG. 4 (56 of 61)

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AAGGCGTGCATATGCATGTAAGTGTGGGTTTTCACCTCTCACCCAAAAGCCT  
 ACTCAATTTTTTACTGCAAAAACATGTTATCATCATTATTTTTTACTTAG  
 CCCACCTTTTCCTTGGCAATTTTCCATAGGAAATGCATTCTAAATTTCAA  
 CTAATCAGGGGACTTGGAGCCTCTGGACACCCCTTGTTCCTTGCCACA  
 GTCCCTTGCGAAGGTCCTTATCAGAGCGGGCTCCATGCGGGGCTCAGG  
 ACAGGATCAGATGTCAGTTGCACCAAGGGGACGGGACAGATCCTCTCTG  
 CTEACCATGCAGAAGGGACTGTTTCAGTGCACCGTCATGGTCTGGTGATT  
 TCTGGTCCATAAGGGAATTTTCACATGCATCGGGTGATTGTCACATCAGC  
 ACAACACTGTGAGGAAGGCAGAGTGAGAATTTGTGTGCCCATTTTATAGG  
 TGAGAAAACAGATGCAGAGACATTAAGTAACTTCACCACAGTCATGCGGG  
 TTTTAAAGTGGCAGACTTTCAGGTGTTGTGACTCCTAGTCCAGAGTCTTT  
 GCACTGCCCTGAGGTGCTAAACTCTACTGTGCTTTAAGACTCACTTGG  
 GGAGCTTCCATAAAGAGAGGATTCACAACCTGAGATTCTTGTTTAACTG  
 TTTTGGGATGTAGCTCAGGAGTCTAGCTGCCTTAAAAAATAAACTCCA  
 AGTAATTCTGATGCAAGCGGTTCTTTTTGTCCACCTTTGAAGAAACACT  
 GCCTCCTCCCATACATTTTCATTAGAAAATGGTAACATGTTTTCAGCCT  
 GAGAGCCATTTCTGGGTGACCGGACGTGCGCAGCCCGCTGTACTAGCTTT  
 CAGTCTAGGCTTAAACACACATGATAGGAGATGTCCTACTCCAGATGATA  
 TGAGTCTGAACCATGGAAAAATTCATTGTGTGGCACATCTGGTGGGTGT  
 GCACTGTCCCCAGCAGTGAGGCCACCCAGTGAAGACAGCAGCTGGGAGAGG  
 CTTAGTTACATGCAGTGGGACAGTGTGGGCTAGACTGCTGAGCCCTCTGC  
 AGTTTACTCTGTGTGAGGCAATGAGGGTGAAGGCTGATCAGACCCAGCT  
 GCAGACCATAACCCTCCAGGGAGACAGATATCAGTCAGGACAACCCCAAGT  
 GTAGCTGGAGAAGCAGTGCCACGGTATGACCGGATGTGTATCCAACCAGG  
 AAATCTGCATATAAATATAAGAGGAGAAAAATGAACAGATGTTGCTCTTAT  
 ATGTAGATATTTATGAAGAGCATATAATTTTGTGTTTGTGTGTTTAAAGAA  
 GTTTATAAGTATGCCTTAAAAATGTATAGTATATACTGTAGGTATTTTTT  
 CCATTAGATATTTTGTTTTTTTCATCTATTATCCACATGCATTGTAGCAAC  
 AGTATAATATAACAACCTCCTCTACAAAAGCAGAAGGAAGTGAAGCTTTG  
 GAAGGAAGCACCCAGTGAGCTTGCCCTTTTCAGGTGGGTGCAGTGAGCAG  
 GAGTCAGTGAGGTTGAGATCCTTTGAGAGGAGGCAATCATTAACCAGGAA  
 ATCTGCACTGCATCCTGGCCACACCTAACCTTGACAATGGTGCTTGGA  
 GCGCCTTCCAGCTCTTAAGGCTTGCGATTCTTTCTCTCACTCTTCACCC  
 ACGATGATTAATCTTCTCTACAGAGTTGGACAATAAAGCCTTGAGTTC  
 CTGCCTCCCCTGGTGTGATCAGGAGCATAGACATGGCCAGGAACATGTA  
 GGTGCTTTGAAAGCTGAACAAGTTAGTAAATTCAAACCTCATTTCACC  
 CACCGAGTAAATGGGAATAATAATAAACCTATTTTACATAGGGTTGACAA  
 GAGGAGTAAAGAGGGATTCAATGAAAGTTCGTTATTATCATTGTAGTAG  
 CAGTGTGATAATATCAACTGAAAGTTCATTATCATTATTAGTAGCAGTA  
 TTGATAACCCTCTTTCTGTGCCCTTCTCACTGGTGGGCCAGGCCATCAG  
 CAATGCCCAGGGTGTGATGGATCTCTGCTGCATCGGGCACCAGCTGTGTC  
 AATGGTGAGAACAGTACAAGGGTGGGCAGGGCAAGGCAGGAAGCACCCAG  
 GAGCAGCAGCTTACATGGGTGAAGATGTCAGGAGCTTAGGGACAGTCAGA  
 GCGGGTGTGCCTCCTCTTTGTGGAGCCTTTCTGCGTGGGTGGAAGTCTGCTG  
 CAGCTGTGGCCATGGATTACCTGAAATATGGGTGGAATTAGGCATTTCAGC  
 TGGGTTAGCTGTGCCTAGAAGGAGGAACTCTAAACTGAGAACTTGTCCCT  
 ATTGCCACCTCTGATAGGCAGATGATCCATCCATCAGTGGCTGAGCTGAG  
 GTGTGCATGGGGATGGGTAAAGAGCCCAACACAGGGCTGATGACTGAGTC  
 TATTTAGAACAATAGATGTAAATCTGATAATGTAAATGTGATAGATTA  
 TTTTGTCAATTAGAAATGGTACCATAAATTATATATATACATAAACATG  
 TATACATATACACATATACATGCTGTGTGATAAACAACACACAGTATTGTC  
 CCTACTCTATTCCATAAACCTGATGCCTTTAGCTGGGATTCCAGCTTTT  
 ACTCTCCTCTCTGTCTCTGCTGTCTATATCCTCCCCATCCTGTAATTCT  
 GGCTTATATGCCACTTCCTCCCTAAAGCCCTCCTCAATCCCTTGCTGGA  
 AGTGACATTTTCTCTTTGAGCTGCCCCCTGCTTGTGCTTTGGTGAGGTCA  
 GCTGTATTGCAGTACCTTGTATTGTGGTTGTACATCATCGTATAGAATT  
 AATTTCTGACACATTCGGTATTTTTCAAAGGGCCTAGTGTGGGGCTTTAA  
 CAGTAACACGCCACCAAGCCCAAGTTAAATTTTGTATTTTGGTGGAGA  
 CAAGGTTTACCATTGTTGGCCGGGCTGGTTTCAAACTCCTGACTTCAGGT  
 GATCTGTCTGCCTCAGCCTCCTGGAGTGCTAGGATTGCAGGCATGAGCCA

FIG. 4 (57 of 61)

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CTGCACCCAGCCACCTATCAAAATTTTAAGTGCCATTTTATTTTATT  
TTTTGTAGAAATGGACAAGCTGATCGCAAATTCACATGGAATTGCAGGA  
GGTTCCAAATAGCCAAACAATCTTGAAAAAGAAGAACAAAGTTGGAGGA  
TTTACACTTTCCAGTTTCAAGACTTAGCTCTTAGCTACAAAGCTACAGTA  
ATCAGAACACTATGGTCCTGGCATAAGTGATGCTGGACAGGTGAGCCCCA  
AAGTGGGACTTAACCTGTGAAGGTTCTTGGCCTTGCCAGGAAGGAATTC  
AAGGGCAAGCCAATGGGACAAGAAAACAGCTTTATGAAGGGGCAGTATT  
ACAGCTCCAGCCCTGTTACAGCTCCAGCCCTGTTACAACCTCTGACTACTC  
CTGCACAGAAGGGCTACCCTGTAGGCAGAGAGTAGCAACTCAGGGCAGTT  
TTGCAGTCATTTATATCCACTTTTAAACATGCGAGATTAAGGGACAATTT  
ATGCAGAAATTTCTACGGAATTGGTAATAACTTTTGGGTGATGGAGTCAT  
CATGGAAAGGGGGCGGGGAACCTCCCTGGTGTGGCATGATGACGGTAAAC  
TGATATGGCGAAGTGGTGGGTATGTCACATGAAAAGCTCCTTCCACCCCA  
GCCCTGTTTTCAATTAGTCTCGGTTTGGTCCAGTGTCCAAGTCTGCCTC  
CAGAGTCAAGTCCACCCCTTACCTCTTAAGGAGAGATGTAAATACATGG  
AATAGAATTGAGAGTCCAGAAATAATCTCATACATCTATGATCAATTGAT  
TTTCAGCAAAGGTGCCAAGACCATTCAATGAGGGAAGAATCATATTTT  
TTCAACAAATGGTGCTGGATAACCATGTGAAAGAATGCAACTGGGCCC  
TTATCTCACACCATAACAGAAATTAACCTCAAAATGGCTCAAACACTTAC  
ATGTAAGAGCTAAAACATAATATTCTTAGAAGAAAACAGGGATATATCT  
TTATGACCTTGATTGCTGGCTGATTCTTAAATGACACTGAAAGCACA  
GCAACAAAAGAAAAAATAGGTAAATTGGACCTCATCAAAATTTAAAA  
CTTTTATGCTGGGTGCACACCTGTAATCCAGCACTTTGGGAGGCTGAGG  
CAGGAGGATCTCTTGAGCCCAAGAAGCTGAGGCTACAGTGAGCCGAAAT  
GTGCCACTGCACTCCAGCCTGGGTGACAGAGCAAGACCCTGTCTCGAATA  
AATAAATAAACAAATATATAATTATAGATCTCTGGATCTTGCTTCCGAG  
ACTGACTCACTAAGTCTGGGTGGGAGCCAGCCATTTGTATTTTT  
GAAAACCTCTCAAATGATTTTACTGTGCAGCCAAGTTGAGAATCACTGT  
ATCATAGGGTTGGACTCCTAACTGGAAACAGTTTGCACCATCAGGTGTG  
CAGCATTCTGATAATAGTTAAGCTTTCTCCTAGATTTTCTGATATTAGA  
TGAGTCATGTTTACAAGTTTTTACCAAGAGACAACTATCTTTCTGCCCT  
TACTTTCTCTTATACTATTCTAATCCAGAACCTTTTGGAACTTCCAC  
TGAGAGATGAATCTAGAAAGTGACTCTCTTGGCTACAACAGAGAGTAATG  
TTGGCCTGTTTGTGCCAGATCCAGTTGGTGGTGGTGGGACAGCACCT  
CCCTGAAATCCCTCTCTCCCGTCAGATTGAGTCCCCCATTTGCATCAC  
GTACAATCATCACTATGGGTTTCTATTACCTTGCTAGGGCATTTGGAGGT  
ACCATATATACCAACTATTAGTTTTGAGCCATGGTTCCCAAAGTGTTGAC  
TGTAAGGGCACCTCAGCACACTCAGAGGTGTGATGGGATATTTAAATATT  
CTGAAGAAAACACAGTGACATCTGTGAGGCCCGTGAAAACCGTTGGCATT  
AAATTGTCTCAACCCCAATTGCTTAAAGAGCAGAACTGGCCAGGCACGGTG  
GCTCACATCTGTAATCCAGCACTTTGGGAGGCCGAGGCGGGCAGATCAC  
GAGGTGAGGAGTTGAGACCAGCCTGACCAACATAGTGAAACCCCGTCTC  
TACTAAAAATATAAAAATTAGCCATGCATGGTGGCATGCACCTGTAACCC  
CAGCTACTCAGGAGGCTGAGGCAGGAGAAATTGCTTGAACCTGGGAAGCGG  
AGGTTGTAGTGAGCCAAATCGTGCCACTGCACTCCAGCTTGGGTGATAG  
TGAGACTACATCTCAAAAAAAAAAATGAGAGAGAGAGAGAGAAGCAGA  
ACCATCAGGTGTTTTCTTTGGCTTAAAGTACTCTGTGAAGAAATTCCTGG  
GACACGAAGGATACCATGAACTGAGAGATTTTGGGAACCTCTGCTTTAGA  
AGCTGGAGGTAGCATTCTTGGGCACAGTACTGCCTTGGGATCAGCAAAT  
CCTTTTGTAGGTGCATTTAGGTGTGGCAAGACAGCTCTTAGAGTGGGACC  
GGGATGTGCTTGGAGACAGAGGGAAGTAGATTGAGCTGCCCGATAAAGAC  
ATGCCAGCCTGGCAGAGTGTAGTGACTCATGTCTGTAATCCTAGTGCTTT  
GGGAGGCTGAAGTGGGAGGATTGCTTGAAGGCCAGGGTTTGAGATCAGCC  
TGGGAAACAACAAGACCTCTACAAAAAAAAAAGAAAAAAAAAATTAACCA  
CATGTGGTGGCATGCACCTGTAGTCCAGCTACCTGGCAGGCTGAGGTAG  
GAGGATCACTTGAAGCCAGGAAGGTAAGGATACATTGAGCCATGACTGTG  
CCACTGCACTCTAGCCTGGGTGACAGAAAGAGACTCTGTCTCAGAAATAA  
ATTAATAAATAAATAAATATATAGTGGCCATGACATCCCTAGAAAGACA  
AGGTCCTGGGAATAGGTAGAAGCCAAGGGAAATGAGAAATGAGAGGGGGC  
CCTGGAGCTGGAAGTGGGGGAGCAGGATGGCCTCTGAGAAGTTCCTGATA

FIG. 4 (58 of 61)

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GTGGTGTCACTGATGTGTCTGATGTTTAGTTGTAATTATTTGCTGGGCCC  
CTGTATCCCTCATATCTGATAGCTCTTTGCTAGTCAAAGTGTGGTCTGG  
GGATCAGCGGCATCAGCATCACTTGAGAACTTGTTAGAGATGCAGAATCT  
AGAGCCCCACCGGGACCCAGAAACAGAGCCTGCATTTTAACAAGCTCCC  
CAGGTGATTCTCACACACACTCGCATTGAGAAAGCACTGGGCTAGTTGAC  
AGATTCTCAGGCATGGCTGACATTGAAATATCCAGGGAGCAGGCTTGGA  
TTAGGATGTTTAAAAGTCTCCAGGTGTTTCTAAAGCCAGGTTTGAGGAA  
TTACTGGGCTGATACAAATGTTTGTGATGATGCTTTGTGTGTGTGTGTG  
TG  
TGGTCACTTGGCACCAACACAGGAAACAATGGAAATATGTGAGCCATGA  
CAGAAAGGTGAGGAGATAAAAGAAATTAGTGACATGAGAGGTACTCCTCA  
GGTGTTAGGAAAGAGGGTAGAGCAAACCAGGTTTTCCACCATATGTTGGA  
TAGGGGGTCAAGTAAATTTCTACTTAAAAATTACAAACAGGGGCTGGGCG  
CGGTGGCTCATGCCTGTAATCCCGCACTTTGGGAGGCTGAGGAGGGCGGA  
TCACAAGGTCAAGAGATTGAGACCATCCTGGCCAACACGGTGAAACCGTG  
TCTCCACTAAAAATACAAAAATTAGCTGGGCATGGTGGTGCCTGCTTA  
TTCCAGCTACTCGGGAGGCTGAGGCAGGAGAATCGCTTGAACCTGGGAG  
GTGGAGGTTCAGTGGGCGGAGATCGCACCCTGCAATCCAGAGCGAGAC  
TGTGTCAAAAAAAGAAAAAAGAAAAATTCCAAACAGGATGACCTAAG  
CCTGCAGGACTTGGAGACATCTAGGTGACTGATACTCAGTCACAAAACAT  
AATTGGTCACAGGCCTGATGAAATGCACAGCAGACCTTCAGATGGTATGC  
ACTCAAGTGATATCCACAAGTCCACCTAAAGAAATGCTATATTCAGACAT  
TTGGCATCAATCTCTATCAACAAAGATAGTCCAAAGCAATGGGTTCCAA  
AAACACTTTCTAAGACAAATTCTCTATTTGCTTTAATATCAGTCATCC  
CAGCCCTTGGAATAGAGGAGCAAATGATACCAGTGGTACCCTACCACAAT  
GCACCAAGGTATTATCTCTCATGCTCCATTTCTCCCTCTGTCTACATC  
ACTAATAACTCATTGATTTCTGGTGCAAGCCCTGCTGGGAGAAAAAGTCT  
ACTCTGTACCTTGGAGCAAGTTGCTCAGAGTAGGTATCGAGGATAAAAT  
TTGGAAGTTAGAAAAGCTATTAGAAGGAGATCCTAGTAGTTGAAAACAC  
AGCCTGGCCAAGTCAATGATGCTATTTCTCTCCCGAGCCTTGCTATGTCC  
ATAGCTAAGGAAGACAATTTAGGCTTGGGCTAGAGGATGGGAAAGGGCAA  
AATTACTGATGCCACAGCCAGAGAGGTATTCTAGTAATCTGAGGGTGAG  
GACCACATACCTGGTTGAGGACGTACAGTGTGACAGCTGTGAGTGGAT  
GCCTGGAGTTCTGGCGTGTCTTCTAGCACAAATGATACCTGAGACTCTTGC  
ATCATTGGGAATAATAAAATGGGAGTGGATAGATATGAAATTATGATGGC  
AATAAGCAATCAGCTAATAGCTTCATTGATGGGACAGATTAAAGATGGCT  
GCAAATCCTTTGGTCCAGGTTTGGGATATAGGCAGCATTGTATTGGAAT  
GCTGATAGTCTGAGGCCATGAAAAGTCCACCTGCAGTAGTGGTAGGAGGA  
ACAAGCCTCACTTTCTTCAATGTGTGTGACTGCTGTCTTGATTCCCTGGG  
TGGCCAGTTCATTCTGTGTGGTTCTTTGGTCCACTTGACTCTGGGGTGGC  
TCTGTGATGGCTTGACCAATACAATGTAGTGGAATGATGCTGTCTCAT  
TTCCAGCCTCTTCCAGCCTTAAGGAACTGGCAACTTTTATTTCTGTCCCT  
TGGAATACTTGTCTTGCAACCCATCCATCATACAGTGAGAAATTCTAAG  
CTGCCCCATTAAGAGGGCCACATGGTGATAAATTGGGGTCTTACATACAG  
CCCTAGCTGTGCTCCTAGCTGACAAACAGTAGCAACTTGTCAACAGGCGA  
GTGAACCACTTAGGACTGTATACTCCAGCCCCAGTTGAGCAATGTGGAAC  
AGAGTAAACCATCTCAGCTTAGCCCTGCCCAAAGTGCAGAAATTATGAGCA  
AAATAATCCCCTAGGCTTTGGGCTGATTTGTTCCAGATTACTGGAACAGA  
ATTTGGTACCAGGGGTGAGGTGCTACAGCAATGAAAGCTTAAGACACGTG  
ACTTTGGTTTTGGGTCTGAGTGGCAGGGGAACTTGGCAGGCCTCAAGGAA  
ACTTTTAGGGAGGGTTGAAGCATAGTGAGGAAAACAGTAGGGGAAAGCTAG  
AGGAAAAAATGATGCTTGGTATGTAGTGGTGGGAAGTTTAGCAAACTCG  
CCTGATGTAATGTGGGAAATTGTAAGAACTCAGAACGATTTAAGGGCATG  
TTTTATAGGTCCTTTAAGAACTTCTAGGCCAGGCGCAGTGGCTCATGTC  
TGTAATCCCACTTTGGGAGGCTGAGGTGGGCGGATCACAGGTCAGG  
AGATCGAGACAATCCTGGCTAACATTGTGAAACCCCGTCTCTACTAAAC  
TACAAAAAATTAGCCGGGCATGGTGGCGGGTGCCTGTAGTCCAGCT  
ACTAGGGAGGCTGAGGCAGAAGATGGCGTGAACCTGGGATGTGGATCTT  
GAAGTGAGCCAGATTGTGCCACTGCACTCCAGCCTGGGCAACAGAGTGA  
GACTCCGTCTCAAACCGAAAAAAGAAAAAAGAACTTCTAGGGC

FIG. 4 (59 of 61)

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TGGTCCCGTGAAGCCTCACACATGGTACACAAAGGCTGTCTTGAAAAGA  
AACGTAAGTGTGTTTTTTGGTTTAATAAAATTGATTATAAATGGATAATG  
CAAAACATTTTAAAGAATTTTACTAGCTTACATTAGCAGATTTGGATCCA  
GTGATTGTTACATTCTGGTACTGAGCCCCTGAATTACTTCTTTGAGTAAG  
GCATTATACCAAAGCTATTGATAGTTGGGCTTATAGGGTGTATGTTTGAA  
GAACTACTAATGTCAAAACCAATATTTACGGTTCGACAAGAGGACATCAG  
AACTGGTAATCCTTATTACCATGACTGGCTGGACAGAATACTCAATGTAA  
TGGGATTTCTCTGCAAAATAAGACGGGGAAGATGTAAAAAGATGCCTGAA  
CATTCAACATTAATGAAAGATTTTCAAGAAGAAATATGTATACTAACTGCAG  
CCTTATCAAGTATATGGAAAAACACAAAGTTAAACCAGATAGTAAAGCAT  
TCCACTTGCTTCAGAAGTTTCTTACTATGGACCCAATAAAGTGAATTACC  
TGAGAACGGGGTCCCTGTTTCTTCGAAGACCCACTTCCTACATCAGACGT  
TTTCAACAGTTGTCAAATCCCCTACCCAAAATGAGAATTTTAAACAGAAG  
AAGAACCTGATGACAAAGGAGCCAAAAAGAACCAACCGGCAGCAGGGC  
CATAACCAACGAAATGGAACTGGCCACCCAGGAATCAAGACAACGGTCAC  
ACACAGGGGACCCCCGTTGAAGAAAGTGAGGCTTGTTCCTCCTACCACTAC  
CTCAGGTGGACTTTTACGGCCTCAGACTATCCGCGTTCCAATCCACATG  
CTGCCATATATCCCAACCCTGGACCAAGCACATCCCAGCCGAAGAGCAGTG  
TAGGATACTCAGCTACCTCCCAGCAGGCTCCACAGGACCCACGTCAGACA  
CACGGGTACTGAGCTGCATCGGAATCTTGTCCGTGCACTGTTGTGAATGC  
TGCAGGGCTGACTGTGCAGCTCTCCGTGGGAACCTGGTATGGGCCATGAG  
AATGTACTGTACAACACACCTGCCAGTAGCCAAGTTCCTTCCACCGCT  
TTTACAGATCGGGGTAGTGGCTTCCAGTTTGTACCTATTTTGGAGTTAG  
ACCTGAAAAGAAAGCGCTAGCACAGTTTGTGTTGTGGATTTGCTACTTTC  
ATAGTTAACTTGACCTGGCTCAGACTGACCAGTACTTTTTTTCCGTGAC  
AGTCTATAGCAGTTGAAGCTGAGAATGTGCTAGGGGCAAGCGTTTGTCTT  
CATATGTCATGAATTCCTCCAGTGTAAACACATTATCTGACCAATAGTAC  
ACACACAGACACAAGGTTTAACTGGTACTTGAAAACATACAGTAGGTGTT  
AACTCAGTGAAATAACCAGGACTCAAAGTAAGATTATTTTGGTACACCTT  
TCTTGTTAGTGTCTTATCAGTGAGTTGATTCATTTTCTACATTAATCAGT  
GTTTTCTGACCAAGAATATTGCTTGGATTTTTCTGAAAGTACAAAAAGCC  
ACATAGTTTTTTTTCAGAAAGGTTTCAAACCTCCTAAAGATTAATTTCCAA  
GTATAAGTTTTGTTTTTATTTTCAATCTATGACTTGACTGGTATTAAAGCT  
GCTATTTGATAGTAATTAGATATATTCTCATTGATATAAACCTGTTTGGT  
TCAGCAAAACAACTAAATGATTGTACAGACAATGCTTTATTTTTCTTG  
TTGGTGTGCTTGTGGGAAAAAGAAAGAGAGATCAGATTGTTACTGTGTC  
TGTGTAGAAAGAAGTAGACATAGGAGACTCCATTTTGTCTGTACTAAGA  
AAAAATTCTTCTGCCTTGAGATGCTGTTAATCTATATAACCTTACCCCCAA  
CCCTGTGCTCTCTGAAACATGTGCTGTGTCCACTCAGGGTTAAATGGATT  
AAGGGCGGTGCAAGATGTGCTTTGTTAAACAGATGCTTGAAGGCAGCATG  
CTCGTAAGAGTCATCACCCTCCCTAATCTCAAGTACCCAGGGACACAAA  
CACTGCTGAAGGCGCAGGGACCTCTGCCTAGGAAAGCCAGGTATTGTCC  
AAGTTTTCTCCCCATGTGATAGTCTGAAATATGGCCTCGTGGGAGGGGAA  
AGACCTGACCGTCCCCCAGCCGACACCCGTAAAGGGTCTGTGCTGAGGA  
GGATTAGTATACGAGGAAGGAACGCCTCTTTGCAGTTGAGACAAGAGGAA  
GGCATCTGTCTTCTGCCCCGTCCCTGGGCAATGGAATGTCTCGGTATAAAA  
CCCGATTTTATGTTCCATCTACTGAGATAGGGGAAAACCACTTAGGGCT  
GGAGGTGGGACATGCGGCAGCAATACTGCTCTTTAAGACATTGAGATGTT  
TATGTGTATGCATATCTAAAGCACAGCACTTAATTCTTTACCTTGTCTAT  
GTTGCAGAGACCTTTGTTACGTGTTTATCTGCTGACCTTCTCTCCACTA  
TTATCCTATGACCCTGCCACATCCCCCTCTCCGAGAAACACCCAAGAATG  
ATCAATAAATACTAAGGGAACCTCAGAGGCCGGCGGGATCCTCCATATACT  
GAACGCTTGTCCCCTGGGCCCCCTTATTTCTTTCTATACTTGGTCTCT  
GTGTCTTTTTCTTTCCAAGTCTCTCGTTCCACCTAATGAGAAACACCCA  
CAGGTGTAAAGGGGCAACCCACCCCTTATTGCTGATTGTGAGCGTGCT  
TTAAGGTGAAAAAGCATGAATGTTAACTTCCTTAAAAAGGTACAGCATC  
CAATTCAAATTTTTTGTCTGATTTTAAATGCTAGTTGATGTAGTGCTAT  
TAAAAATTTGTTCAACATGGACACAGAGAGGGGAACAACATACCAGGG  
CCTGTTGCGGGGTGGGGATGAGGGGAGGGAACTTAGAGGACAGGTGAACA  
GGTGACGAGATCACCATGGCCACATATACCTATTAAACAAACCTGCAC

FIG. 4 (60 of 61)

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GTTCTGCACACGTATCCCATTTCTTTTTTTTTTAAGAAATAGAAAAAA  
AATAAAATTTTGTTCACTGATTCTTCCATTTTAAACCTTGTTTGCATGTG  
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AATTTTTGAGGGAAAAAAACCTATAACATACATTGTACTGTATCAAACCT  
ATTTTACATGAATGACACAAGTATTCTGAATAAAAAAATAATTGAACATT  
GTTAAGAACAAGGTGTCATGTAATTTATTTTTTCATAAATAAAAAAATTAT  
AGTGGCTTAGACTGAAAGGAACAGAGAATTTAAAAAATTAAAAAGAAGCC  
TTAGTATATTTTTGTATATAGTTTCCATGTGCCATATTTGCCATAATTGG  
ATGAGAATTTTTTGACCTCTGGCAGGGTGACCCTATATTTTCANTNTATA  
AAGCGTGCATCATACC

MVLKCHPPTGDSQCAIPGVRVTALGHATQRVSSIXQIIPQI.WECIRKTEAWIIHPII.I.NISI.QPQIGI'CSL.SNKCI.SSI.QRSASA  
E:KGSPII.I.GVSKGEFCL.YCDKDKGQSIIPSI.QI.KEKI.MKI.AAQKESARRPFIYRAQVGSWNMI.ESAIIPGWIFICTSCN'N  
I:PVGIXNXVDIPI.I.GKAQKRGTCSE

FIG. 5

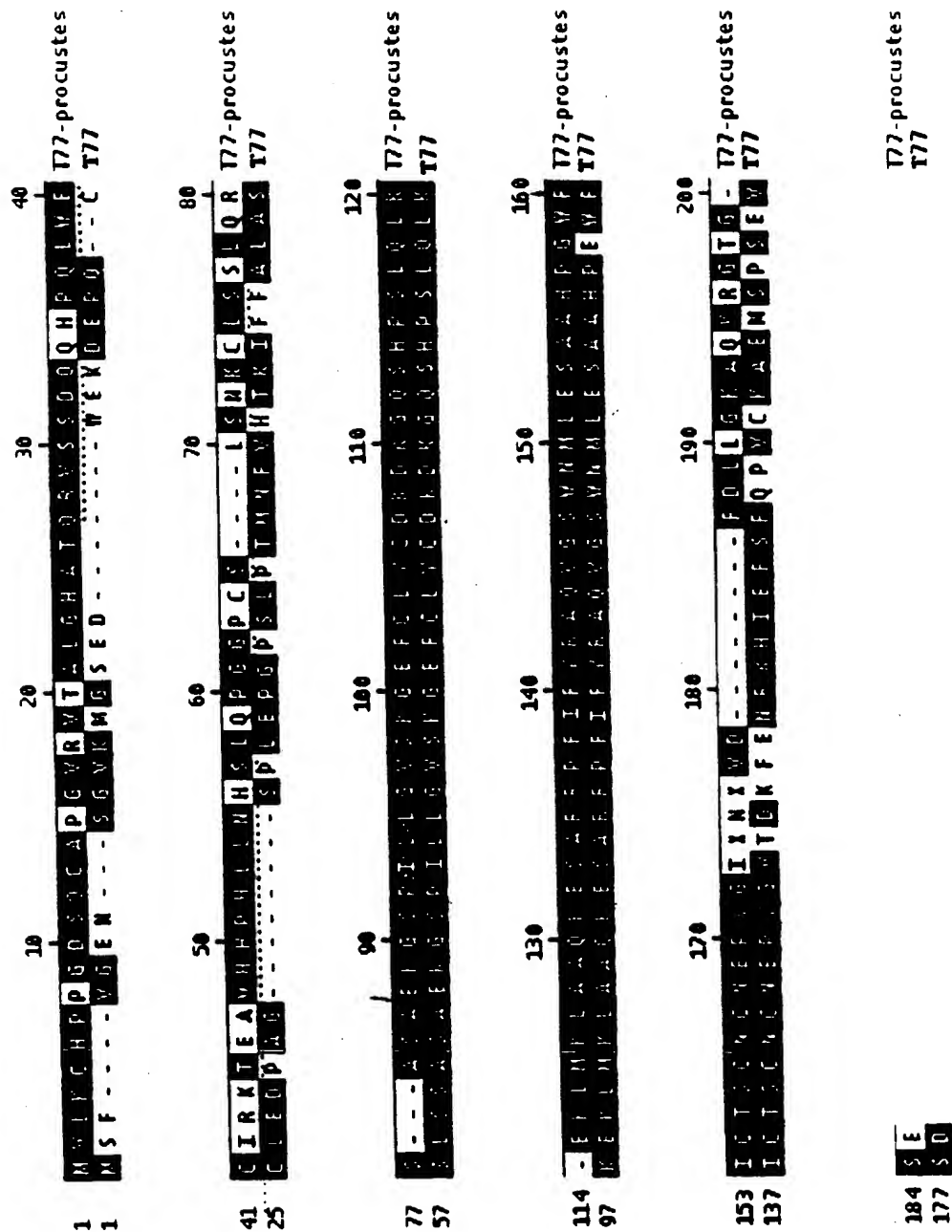
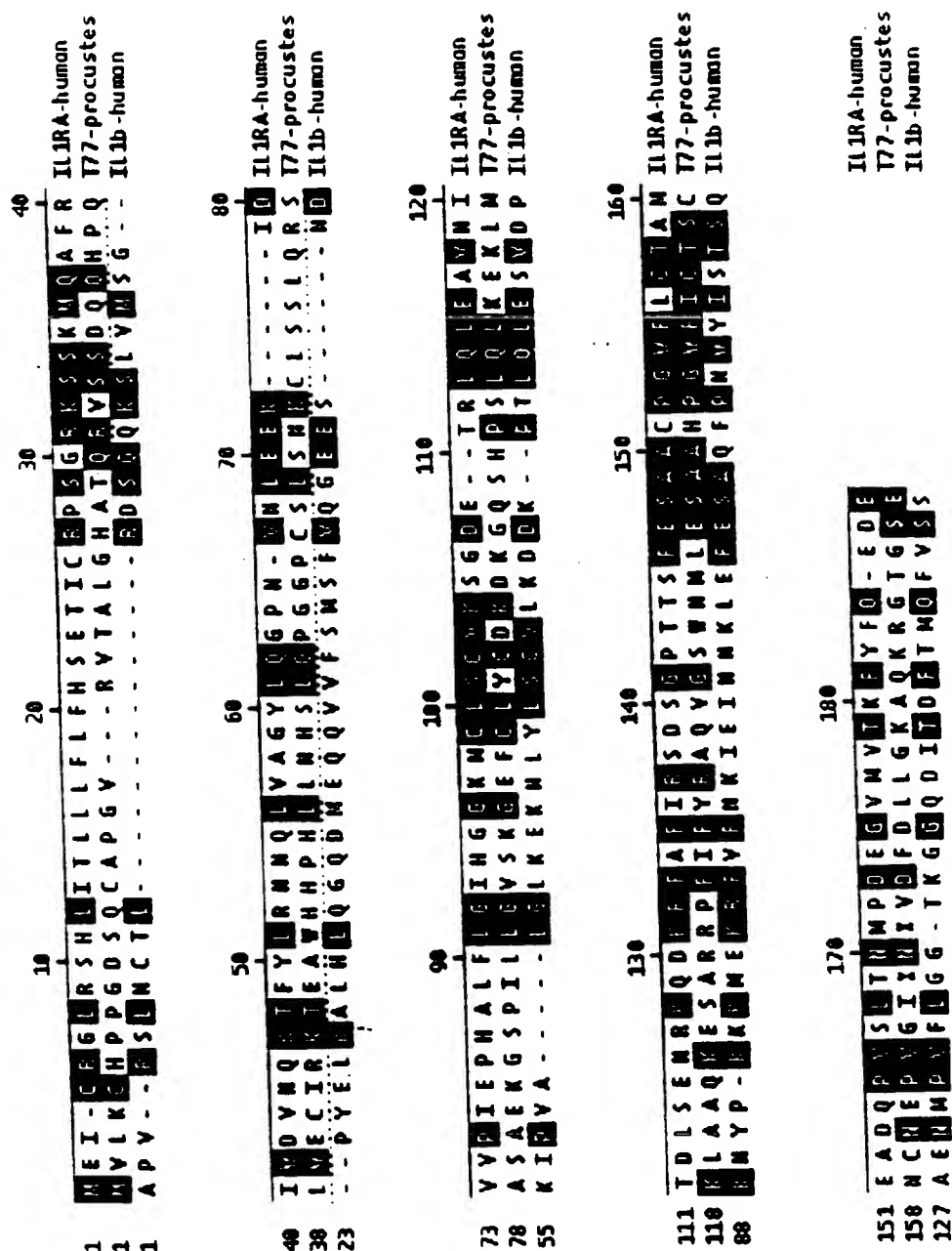


FIG. 6

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**FIG. 7**

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US98/16102

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC(6) : C07H 21/02, 21/04, 1/00, 14/00, 17/00; C12Q 1/68; G01N 33/53

US CL : 536/23.1; 530/350, 387.1; 435/6, 7.1

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 536/23.1; 530/350, 387.1; 435/6, 7.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

DIALOG: MEDLINE, USPATFUL, WPI, BIOSIS. Search terms include author, "TANGO" and protein

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	Database Medline on Dialog, US National Library of Medicine, (Bethesda, MD, USA) AN 09370320. SONNENFELD et al. 'The Drosophila tango gene encodes a bHLH-PAS protein that is orthologous to mammalian Arnt and controls CNS midline and tracheal development'. Development. November 1997, volume 124, number 22, pages 4571-82, Abstract.	1-22

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:	*T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
*A* document defining the general state of the art which is not considered to be of particular relevance	*X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
*B* earlier document published on or after the international filing date	*Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
*L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	*A* document member of the same patent family
*O* document referring to an oral disclosure, use, exhibition or other means	
*P* document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

21 OCTOBER 1998

Date of mailing of the international search report

30 OCT 1998

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